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Original Communications

Department of Clinical Reports

Department of Reviews and Abstracts

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The American Heart Journal

VOL. 15 MAY, 1938 No. 5

Original Communications

A COMPARISON OF PERCUSSION AND RADIOGRAPHY IN LOCATING THE HEART AND SUPERIOR MEDIASTINAL VESSELS*

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STATEMENTS in anatomical and clinical textbooks regarding the position of the cardiac borders commonly have several defects: failure to distinguish between the living subject and the cadaver, failure to make allowance for normal variation, and failure to indicate what or how many subjects provided the average figures that are quoted. Certain cardioradiologic data fulfill these requirements, but cannot be used as standards in percussion unless the discrepancy between percussion and radiologic observations is well known. In our department percussion is used as a method of "dissecting" the living body, and the question of its error has naturally arisen. Although many informal investigations on this must have been carried out, there do not appear to be many published reports. Examples are those of the following authors:

Bisbini,[1] after comparing orthodiagraphy and five percussion methods on eleven persons, concluded that percussion figures were often a little smaller than those obtained by orthodiagraphy. The data show that greater allowance for variation ought to be made than the author apparently realized.

Kurtz and White[4] compared teleoradiography and percussion on one hundred patients (adults and children, males and females). Their data suggest that the low average percussion error and insufficient analysis of variation led to the conclusion that percussion was "reasonably accurate."

Wilson[8] made a general statement of Gordon's special study, and his conclusion was that the percussed outline agreed with the roentgenogram if the patient was standing, but was quite unreliable in recumbency.

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Submitted for publication Jan. 5, 1938.

Further investigation is justified by the not uncommon distrust of percussion piquantly expressed by Wilson,[8] and by the fact that, percussion being an art, detailed studies by many observers are necessary for a verdict on its general reliability.

OBJECTS OF THIS INVESTIGATION

"Percussion error" is used here in its clinical sense, as meaning the difference between percussion results and those of teleoradiography, the latter method being accepted as the standard, more reliable than percussion, but not necessarily perfect. Our objects were (1) to find the discrepancies between teleoradiography and one common percussion method used by an experienced physician (not a cardiologist) under favorable conditions, that is, avoiding females because of the mammary gland, diseased subjects, and stout middle-aged or old men; (2) to search for factors such as chest shape that might enable one to estimate the percussion error in an individual patient; (3) to show what a practitioner could learn of his own percussion error from a small inexpensive series of films.

SUBJECTS AND METHODS

One hundred ten Dalhousie University male students were used; their ages ranged from 19 to 25 years, except for three between 25 and 32 years. Some were Anglo-Saxons, others American Hebrews of varied European ancestry. In all students the same physician found the deep dullness of:

(*a*) the superior mediastinal vessels and heart in the first five intercostal spaces on the left;

(*b*) the heart in the fourth right intercostal space;

(*c*) the liver, approached from above, in the right midclavicular line. The physician placed his left middle finger flat on the chest parallel to the border of the organ that he was approaching, and struck the terminal phalanx of this finger by the tip of the right middle finger. He marked by skin pencil the dullness at each of the points mentioned above and fastened by adhesive tape along the pencil mark a brass wire ½ to ¾ inch long and $\frac{1}{32}$ inch in diameter.

During percussion and filming, the students were always in the midphase of respiration with their arms loosely at the sides of their bodies. Each student was first percussed erect, and then a heart radiograph was taken with the student's anterior thoracic wall against the film holder, the x-ray tube (G.E.C. line-focus, mechanically rectified, 100 Ma., 100 kv.) being 6 feet from the film and centered about the fifth and sixth thoracic vertebrae. The wire markers were then removed from the chest wall, the student lay down, percussion was repeated, new wires were attached, and a radiograph was taken with the film beneath the student and the x-ray tube 6 feet above the film.

On all the films one observer (C. B. S.) measured with calipers, to the nearest millimeter, the perpendicular distance from the center of the shadow of each wire to the adjacent border of the heart, vessel, or liver. If the wire representing deep dullness lay within the shadow of the organ, the measurement was marked +, if outside the shadow, –.

Biometrical analysis of such data is necessary, and the frequency distribution of the errors, as in Fig. 1, was of the "cocked hat" type, sufficiently like a statistically normal curve to justify testing the results by normal curve methods. We adopt the usual convention regarding the significance of differences previously discussed in another connection (Mainland[5]) and more fully treated elsewhere (Mainland[7]),

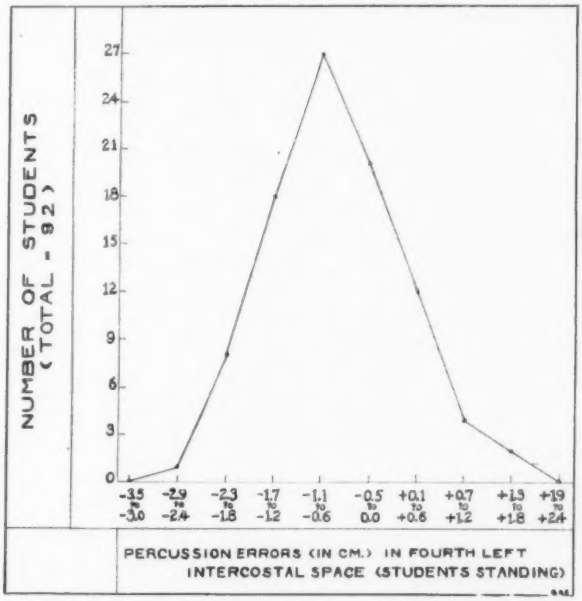

Fig. 1.—Frequency distribution of percussion errors.

along with the other statistical methods mentioned below. (It should be specially remembered that "significant" does not imply "important.")

MEAN PERCUSSION ERROR

Erect Position.—The mean percussion errors in intercostal spaces L 1 and L 2 (Table I) are less than twice their standard errors and therefore not significantly different from zero. In the other spaces the means are all much more than three times their standard errors, and this is very strong proof that under the given conditions the shadow of the percussion marker tends on the average to be lateral to the radiographic border in spaces L 3, L 4 and L 5 by over half a centimeter, and in space R 4 medial to the radiographic border by about 1⅓ cm.

Recumbent Position.—Except in L 2, all the mean differences are definitely significant. In each space they are in the same direction (+ or −) as in the erect position. For each student the error was compared with the corresponding error in the erect position, and in the upper four left spaces there was no marked discrepancy between the two positions, but in L 5 and R 4 the errors were significantly greater in recumbency. The average differences are shown in Table I.*

TABLE I

PERCUSSION ERRORS IN PRINCIPAL SERIES OF STUDENTS

(The + and − Signs Are Used as Stated in the Text)

INTERCOSTAL SPACE (RIGHT OR LEFT)	STUDENTS STANDING ERECT				STUDENTS RECUMBENT			
	NUMBER OF STUDENTS	MEAN ERROR (CM.)	STANDARD DEVIATION OF SERIES OF ERRORS (CM.)	STANDARD ERROR OF MEAN (CM.)	NUMBER OF STUDENTS	MEAN ERROR (CM.)	STANDARD DEVIATION OF SERIES OF ERRORS (CM.)	STANDARD ERROR OF MEAN (CM.)
L 1	93	+0.157	0.803	0.083	94	+0.262	0.826	0.085
L 2	93	+0.057	0.886	0.092	94	+0.157	1.036	0.107
L 3	93	−0.579	0.912	0.095	94	−0.435	1.190	0.122
L 4	92	−0.661	0.907	0.095	93	−0.711	1.074	0.111
L 5	90	−0.582	0.970	0.102	85	−1.307	1.112	0.121
R 4	93	+1.302	0.950	0.098	94	+2.110	1.031	0.106

If sign and degree of error are considered, Table I suggests a certain trend from space L 1 downwards in both erect and recumbent positions, and, in spite of irregularities, a regression test showed that this was more than is usually attributed to chance. In the upper spaces percussion (in recumbency at least) failed to detect the dullness as soon as it should, according to the radiographic shadow, and below that there was a tendency for the dullness to be detected farther and farther away from the radiographic margin. The results of Kurtz and White[4] suggest a similar tendency.

VARIATION IN PERCUSSION ERROR

A low or negligible mean error does not indicate that a method is reliable. The important question is: By how much does the error vary (a) from subject to subject and (b) in repeated examination of the same subject? The variation between students is expressed by the standard deviations in Table I—between 0.80 and 1 cm. in the erect position and rather over 1 cm. for most spaces in recumbency. In such applied biologic work as this, it is customary to use as a measure of uncertainty twice the standard deviation on each side of the mean. If

*Kurtz and White[4] decided that there was no great difference between the error in the erect and recumbent positions. It is not clear whether their averages were formed by summating without regard to + and − signs, but the general average of their hundred subjects may be quoted here for comparison: Space L 4, 5, or 6: 0.6 cm.; L 3: 1.2 cm.; L 2: 1.3 cm.; R 4: 0.8 cm.

Our general conclusions regarding the absence of great discrepancy between erect and recumbent errors agree with those of Kurtz and White[4] rather than with those of Gordon as reported by Wilson.[5]

a physician whose percussion has the variability represented in Table I finds in an erect patient the deep cardiac dullness in space L 4, he has obviously no right to the confidence that the low mean error suggests. For all he can tell, a film taken under the conditions of our investigation may show the radiographic border anywhere from about 2.5 cm. medial to his percussion marking up to 1 cm. lateral to his marking, and in about 5 per cent of patients the difference will be outside even these limits. The actual data used in Fig. 1 confirmed these estimates, and estimates for the other spaces can be made in the same way.*

FALLACIES AND POSSIBLE CAUSAL FACTORS

1. *Dispersion of X-Rays.*—Although radiologic results were adopted as our standard because they are known to be more accurate than percussion, x-rays, even with the tube 6 feet from the film, are not parallel,

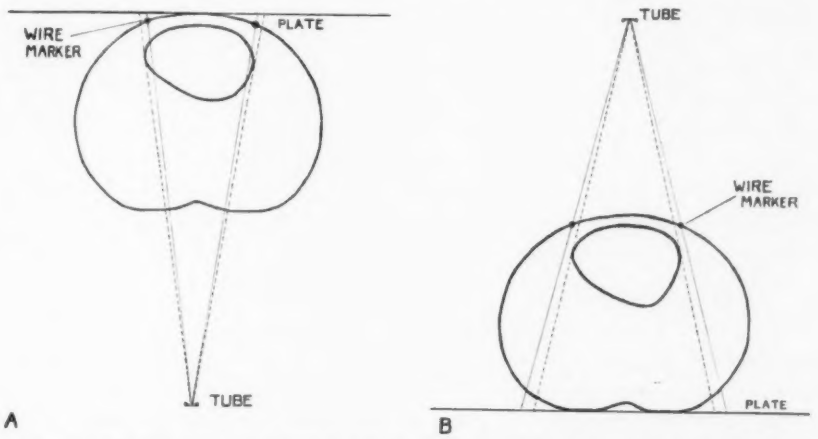

Fig. 2.—Outlines of thorax and heart to show effect of dispersion of x-rays. *A*, Students erect; *B*, students recumbent. Plate = film holder. (The distances between tube and thorax are diminished out of proportion to the thorax size, to fit into the diagram.)

and the question arose: Could the dispersion of the rays account for the mean percussion errors, or for the differences between the mean errors in the two positions of the body?

Fig. 2 shows that, if percussion identified exactly the borders of the heart or vessels, their shadows would overlap the shadows of the wires in the erect position (*A*), but in recumbency (*B*) the reverse would be true. In both positions, however, the direction (+ or −) of the corresponding errors was the same (Table I). Therefore the dispersion of the rays could not account for the errors, although it would necessarily affect their numerical values.

*It is unfortunate that the variations in the series of Kurtz and White[4] are expressed only as maximum values outside and inside the heart shadow. In 42 adults their maxima were: Space L 5, 2.1 cm. outside and 1.7 cm. inside; space L 3, 1.1 cm. outside and 3.4 cm. inside; space R 4, 1.1 cm. outside and 4.4 cm. inside. These figures suggest that more detailed data or a more adequate expression of the variation might reveal variation similar to that of our series.

Thirty wires, 1/64 inch in diameter, were mounted at 1 cm. intervals on plywood, and a radiograph of this with the tube 6 feet from the film showed that the following allowance should be made for magnification: For an object (cardiac border or wire) at 5 cm. from the film, 3 per cent; at 14 cm., 8.5 per cent; at 19 cm., 11.5 per cent. It was sufficient for our purpose to apply these figures to the mean anteroposterior thoracic diameter of the students (19 cm. at the fourth costal cartilage) and to use the relative positions of the heart and chest wall given by dissecting room material and anatomical pictures. The results showed that, if there were no dispersion of rays, the percussion error in space L 5 (erect) would be of the order of –0.8 cm. instead of –0.582 cm. (Table I) and –1 cm. instead of –1.307 cm. in the same space in recumbency.

These calculations, although rather rough, showed that the discrepancy in space L 5 between the mean errors in erect and recumbent positions could be accounted for largely, or perhaps wholly, by dispersion of rays. It was doubtful whether the discrepancy in space R 4 could be entirely so explained. Differences in the distance between the heart borders and chest walls in different students might account for some of the variation in error and for some of the difference in variation between the erect and recumbent positions, but we had not sufficient profile radiographs to show this. It was beyond our purpose to pursue this question farther, and the corrections just mentioned need not be considered in the subsequent analysis of the errors.

2. *Change of Position of Wires Between Percussion and Filming.*—For various reasons, chiefly the physician's and radiologist's lack of spare time, it was practically impossible, except on a few students, to measure the position of the percussion markers on the students' chests before filming. Moreover, to secure quietness, percussion was done in a small room several yards from the x-ray room, and the students had to walk into the latter and take up the proper position again for filming. It was therefore necessary to ask: How far did the change in position of the wires due to respiration or skin movement introduce an apparent percussion error?

The midphase of respiration does not secure exactly the same degree of chest expansion on any two occasions, but we should expect that the difference would be as likely to decrease as to increase the percussion error and therefore would make little difference in the mean error. The respiratory movement of the wires might, however, increase the variation in errors, and this possibility was specially examined. On the chests of ten students (Special Series I), percussed erect, measurements to the nearest millimeter were made from the median plane to the percussion wires. On the films, taken after the students had moved about and breathed, the measurements were repeated in each of the six spaces as in Table I, the median plane being determined by the shadows of

wires that had been placed vertically at the center of the upper border of the manubrium sterni and at the center of the xiphisternal joint. All the films showed two or more intercostal spaces in which the thoracic and film measurements differed by no more than 1 mm. In spaces L 1 and L 4 the percussion error was estimated (a) from the thoracic measurements and (b) from the film measurements. The two estimates showed no significant differences either in mean errors (tested by the t formula) or in standard deviations (tested by the z formula). (For the technique of these tests see Fisher,[2] and for a more elementary exposition see Mainland.[7])

In another ten students (Special Series II) percussion was done at the x-ray equipment, and the first film was taken with a minimum amount of movement after percussion. A second film, with the same wires in place, was taken after the student had moved about and had breathed several times. Special attention was paid to the distances between the wire shadows in space L 4 and the median plane, and the change in these from the first film to the second was found to be similar to the differences in Special Series I. More convincing still was the lack of a significant correlation between the change in the percussion error and the movement of the wires. There is therefore no apparent reason to reject the results of Table I because of movement of wires between percussion and filming.

3. *Change in Size of Heart Shadow.*—In Special Series II the differences between the percussion errors in space L 4 (erect) on the first and second films were compared with the change in transverse diameter of the cardiac shadow. The coefficient of correlation (0.725) was significant (Fisher[2]) and showed that the narrower the heart became, the more its left border tended to depart medially from the percussion marker. The importance of this hardly surprising fact was indicated by further investigation. The change in heart shadow might be attributed to the following factors:

A. The phase of cardiac contraction, which is said to alter the size of shadow by 2 to 7 mm. (Köhler[3]). As we had no means of investigating this we turned to other factors.

B. Rotation of the thorax. On the main series (films of ninety students) an indication of chest rotation was obtained by measuring the distance between the sternal midline, shown by shadows of wires placed there before filming, and the vertebral midline, seen on the films. There was no significant correlation between the percussion error (in space L 4, erect) and this measurement of rotation.

C. Change in position of diaphragm. In Special Series II of duplicate films the change in height of the left dome of the diaphragm between the first and second films was found by reference to intervertebral spaces. In intercostal space L 4 the coefficient of correlation between the change in percussion error and the change in diaphragm height

was 0.891—a highly significant value. When the marker in the first film was to the left of the heart shadow (a negative error according to the convention used in Table I), this error was increased in the second film in proportion to the descent of the diaphragm; and when the marker in the first film was to the right of the heart border (a positive error), descent of the diaphragm was associated with a corresponding decrease of the error. This correlation could not be attributed to movement of the wires laterally during inspiration because the coefficient of correlation between the diaphragm movement and the change in position of the wire shadows, measured from the midsternal line, was nonsignificant (0.586), as was also the coefficient of correlation between the wire movement and the change in percussion error (0.599).

Therefore the correlation between diaphragm movement and change in percussion error can be reasonably interpreted as a causal relationship. The descent of the diaphragm caused a medial movement of the left border of the heart, and an ascent of the diaphragm, the reverse, with corresponding changes in the percussion error. The effect of movement of the diaphragm on the position of the cardiac borders is well known, but this analysis has shown its importance even when the subject is in the midphase of respiration on each occasion, and the numerical relationship enables us to interpret and analyze the high variations (standard deviations) in Table I.

In Special Series II (erect) the coefficients of correlation between diaphragm movement and change in percussion error were estimated for other intercostal spaces in the same way as for space L 4. The coefficients were:

L 1:	0.283	L 4:	0.891
L 2:	0.233	L 5:	0.707
L 3:	0.742	R 4:	0.880

The first two are not significant, that is, there is no evidence that diaphragm movement has any effect on the variation in percussion error in the upper two spaces. The other coefficients are all significant. This Special Series II was equivalent to a random sample of the students of Table I, and by a well-known technique (see, for example, Mainland[7]) the coefficients can be applied to Table I to estimate what would have been the standard deviations (in centimeters) if no diaphragm movement had occurred between percussion and filming:

L 3:	±0.61	L 5:	±0.69
L 4:	±0.41	R 4:	±0.45

In spaces L 4 and R 4 the variation has been reduced by more than half, in the other two spaces by about one-third.

Two points should be noted regarding these modified figures:

a. The standard deviations in Table I, compared with these reduced values, indicate how percussion increases the variation which is found in x-ray technique itself; this variation arises because diaphragm movement introduces discrepancies between different radiographs taken from the same person, owing to the difficulty of securing the same midphase of respiration on successive occasions—a difficulty that is well recognized by radiologists.

b. Improvement of percussion technique cannot eliminate the variation due to diaphragm movement, but repetition of observations can reduce it. If the variation between percussion errors in a certain intercostal space in the same patient (see below) is represented by a standard deviation of 0.8 cm. and if a physician desires greater precision, he can obtain it by percussing the cardiac border several times at intervals of a minute or two, without allowing the different results to influence each other. During the intervals the patient will breathe and set himself afresh at the midphase of respiration. The mean of four such readings would have a standard error of 0.4 cm. (division of 0.8 by $\sqrt{4}$).

4. *Change in Accuracy of Physician.*—The physician did not see the films until the whole survey was completed. The percussion was done at intervals throughout four months, but no tendency towards a change in accuracy was found. Usually not more than four students were percussed on any one occasion. On three occasions when five or six were percussed, the errors were tested for fatigue effects, but none was found.

RELATIONSHIP OF PERCUSSION ERROR AND BODY MEASUREMENTS

The statures and weights were obtained from the students' health service records. The chest measurements were made, not with anthropometrical accuracy, but by a pelvimeter, so that, if they proved of value, a clinician might easily make them when percussing a patient. Coefficients of correlation were calculated to express the relationship between these measurements and the errors in space L 4, on about 90 students in each instance.

The numerical error, regardless of its direction (+ or −) had a low and nonsignificant correlation with stature, weight, anteroposterior diameter of thorax, transverse diameter of thorax, height of thorax, and subcostal angle (measured roughly by tracing on paper). When the direction (+ or −) as well as the numerical value of the errors was considered, there was still no significant correlation between the error and the body weight or the transverse diameter of the thorax. There was, however, a slight but definite tendency for the percussion marker to be placed more and more laterally with increasing stature (coefficient of correlation, $r = 0.26$), and with increase in the anteroposterior diameter of the thorax as measured at the fourth costal cartilage ($r = 0.24$). The stature-percussion relationship could not be accounted

for by the slight tendency for taller students to have deeper chests ($r = 0.21$). These slight relationships, whatever their interpretation, have no practical value, but are mentioned as of possible interest to other investigators.

An attempt was made to obtain by profile and oblique radiographs an indication of the thickness of the thoracic skeleton, muscle, and fat overlying the heart, but the results were not good enough to justify an attempt at correlation with percussion error.

VARIATION OF PERCUSSION ERROR IN THE SAME SUBJECT

Kurtz and White[4] stated that thickness of chest wall, age, and sex did not seem to affect percussion error, but it appears to be well recognized that large mammary glands reduce the reliability of percussion, that is, reduce the observer's confidence that he will find the same results on repeating the percussion under the same conditions. We have not a large series of exact duplicates, and the survey did not include females, but our data indicate an answer to the question: Is the variation between repeated observations on the same person any less than the variation, for instance, in Table I, between different people; or is there any factor (apart from major factors, such as, perhaps, large mammary glands or intrathoracic adhesions) that tends to make the percussion error characteristic of the individual student or patient? Three sets of observations provide evidence regarding this:

1. For ninety-one of the students in Table I the error in recumbency was compared with the corresponding error in the erect position. The coefficients of correlation were: space L 1, +0.324; space L 4, +0.376.

2. Through a misunderstanding, seventeen students stood for filming with their arms not properly at their sides. Percussion and filming were therefore repeated. The errors in space L 4 in the duplicate films gave a correlation coefficient of +0.40.

3. In the films of Special Series III the errors of the two physicians in space L 4 showed a correlation coefficient of +0.36.

Both the coefficients in *1* are significant. Those in *2* and *3* taken separately are not, for the samples are small, but all four agree rather closely. They are not large enough to make any reduction of practical importance in the standard deviations of Table I. So far as could be demonstrated, the variation in error in repeated percussion of the same person was, for practical purposes, as great as in the percussion of different persons.

COMPARISON OF THE PERCUSSION OF TWO PHYSICIANS

On ten students (Special Series III) selected at random from those previously percussed (Table I) a second experienced physician percussed the heart and vessels and obtained films as before, but used a method in

which the tip of the pleximeter finger instead of its volar surface was applied to the chest, and the plessor finger struck the region of the terminal interphalangeal joint of the pleximeter finger. Table II shows that in the upper three spaces the second physician's error exceeded that of the first physician to a greater degree than should be attributed to chance. There was a pronounced tendency for the markers of the second physician to be lateral to the cardiovascular shadow in these spaces. It did not appear likely that these differences were due to the aorta, which may cause difficulty in the upper part of the cardiovascular shadow. In spaces L 4, L 5 and R 4 there was no significant mean difference between the errors of the two physicians.

TABLE II

COMPARISON OF PERCUSSION ERRORS OF TWO PHYSICIANS

(The Numerical Differences Were Found Regardless of Whether the Percussion Wires Were Medial or Lateral to the X-ray Borders)

INTERCOSTAL SPACE	MEAN OF DIFFERENCES IN ERROR IN TEN STUDENTS, I.E., ERROR OF SECOND PHYSICIAN MINUS ERROR OF FIRST PHYSICIAN			
	STUDENTS ERECT		STUDENTS RECUMBENT	
	MEAN DIFFERENCE IN ERROR (CM.)	STATISTICAL SIGNIFICANCE	MEAN DIFFERENCE IN ERROR (CM.)	STATISTICAL SIGNIFICANCE
L 1	+1.19	Highly significant	+0.98	Significant
L 2	+1.22	Highly significant	+1.04	Significant
L 3	+1.09	Highly significant	+0.69	Highly significant
L 4	-0.12	Not significant	-0.06	Not significant
L 5	0.00	Not significant	+0.01	Not significant
R 4	-0.21	Not significant	+0.21	Not significant

In spite of its greater mean errors, the second physician's percussion might still be the more reliable if its variation were less than that of the first physician. There was, however, no significant difference in the variation, as shown by the z test. It may be reasonably claimed that the two methods are equally satisfactory, provided that allowance is made for the differences if a patient percussed by the one physician is subsequently percussed by the other.

ESTIMATION OF PERCUSSION ERROR FROM SMALL SAMPLES

In allowing for percussion error, each physician should know the error of his own technique, and yet the expense involved may prevent his using many large films. Decisive results have been extracted above from small samples (Special Series I, II, and III), and similarly an observer may, for instance, compare two methods or test his increase of accuracy after practice. The necessary statistical techniques (t and z tests) have been specified above. They are often simpler than large-sample techniques, they are easy to learn, and the arithmetic for all the intercostal spaces need not occupy more than a page or two of foolscap.

Apart from such comparisons, however, the observer must ask: To what extent may my small-sample estimate of mean error and standard deviation differ from the "true" values of these quantities, that is, those approached by increasing my observations more and more? One example briefly discussed will suggest the answer to such questions.

One set of ten films taken at random from the main series in this investigation showed a mean error in space L 4 (erect) of –0.97 cm.; standard deviation, ±1.45 cm.; standard error of mean, ±0.46 cm. Therefore, on the usual convention regarding statistical significance, the "true" mean error may lie anywhere between +0.07 cm. and –2.01 cm. If the standard deviation remained as above, and the films were increased to 25, the possible discrepancy from the "true" mean error might, on the same convention, be ±0.6 cm.; for a sample of 50 films, ±0.4 cm.; and for a sample of 100 films, ±0.3 cm.

The possible inaccuracy of the standard deviation in this sample is fully discussed elsewhere (Mainland[7]). Regardless of actual estimates, any standard deviation estimated from a sample of ten may be an underestimate by nearly 40 per cent of the "true" standard deviation; from a sample of 25, by 24 per cent; from a sample of 100, by about 12 per cent; and from a sample of 1,000, by 3 or 4 per cent.

With such knowledge the observer may decide that complete cardiac films, to be sufficient in number, would be too expensive, and that he should test his percussion by a fluoroscopic screen or by narrow strips of film to cover the region in which he has found the heart border by percussion.

SUMMARY

The deep dullness of heart and superior mediastinal vessels was percussed on 110 male university students (erect and recumbent) by one physician, wire markers were fastened to their chests, and teleoradiographic films were taken. All results were analyzed statistically.

In these students the mean errors (difference between percussion and x-ray borders) were less than 1 cm. in most intercostal spaces; but much greater allowance for possible error had to be made in percussing any one individual—for example, a range of over 3.5 cm. in the fourth left intercostal space in erect students.

The differences in error between erect and recumbent positions could be largely attributed to dispersion of x-rays.

For practical purposes the variation between two percussions on the same student was as great as between different students because the correlation between the errors in repeated percussion of the same students, although significant, was low.

From one-third to one-half of the variation in the cardiac (but not the superior mediastinal) region was attributable to diaphragm move-

ment, owing to the impossibility of securing the same midphase of respiration on any two occasions.

The risk of wide error in any individual percussion could be greatly lessened by taking the average of several independent readings, thereby reducing the effect of diaphragm movement.

Stature, weight, and chest size or shape had no important relationship to the percussion error.

Ten students, taken at random, sufficed to show the difference in error of two experienced physicians.

Since each observer should know his own percussion error, the amount of information obtainable from a small series of films is illustrated.

We wish to acknowledge our indebtedness to the Banting Foundation of Toronto for financing this research, and to Dr. C. W. Holland, Dr. T. M. Sieniewicz, and Dr. C. M. Jones, of Dalhousie University, for the time and care spent in the percussion and radiology. A summary of part of the work was given at the Oxford meeting, July, 1937, of the Anatomical Society of Great Britain and Ireland (Mainland[6]), and has been incorporated herein with the permission of the Society.

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AN INJECTION PLUS DISSECTION STUDY OF CORONARY ARTERY OCCLUSIONS AND ANASTOMOSES*

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CAREFUL, important, and informing studies on the anatomy, distribution, and anastomoses of the coronary arteries in both normal and pathologic human hearts have been pursued for hundreds of years, ever since Lower first described such anastomoses in 1671. Nevertheless, to this day, in any series of hearts studied from the viewpoint of the correlation of the site of cardiac infarcts and of coronary occlusions, numerous instances of what are apparently inconsistent findings are encountered. It was our purpose to attempt to find an explanation for these apparent inconsistencies. Because of the high incidence of infarcts in the left ventricle, a region obviously supplied by the left coronary artery, most attention is usually given to this vessel. We also at first confined our attention to the study of the left coronary artery. A frequently described finding is marked narrowing or even complete occlusion of one or of several of the main branches of this artery with no definite infarct in the left ventricle, or, at most, some diffuse, microscopic myocardial fibrosis. When this is found, it has been assumed that a collateral circulation had nourished the myocardium ordinarily supplied by that part of the vessel distal to the occlusion. Attempts to demonstrate such collateral circulation by direct, unaided dissection are rarely successful.

Occasionally a heart is encountered in which a fresh infarct is present in the left ventricle, but in which an attempt at complete dissection of all the branches of the left coronary artery fails to reveal the vessel with the freshly deposited occluding thrombus. The most that is found is marked arteriosclerotic narrowing in one or several of these branches. Then one of two assumptions is made. Most commonly, spasm, with temporary complete occlusion of the narrowed zone, is postulated. From the structure of the narrowed arteries, this explanation is difficult for the histologist to accept. He is more often ready to admit that his dissecting scissors may have dislodged a small thrombus from a narrowed area. For this reason, when seeking areas of complete occlusion, some prefer to use multiple, closely spaced cross sections of coronary arteries for routine dissection.

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Noteworthy contributions, nevertheless, continue to be made by careful ordinary dissections. Thus, in the recent publication of Saphir, Priest, Hamburger, and Katz,[1] careful, complete dissection of the main branches of the uninjected coronary artery tree led to the significant conclusion that "wherever a myocardial infarct was encountered, at least two branches of the coronary arteries supplying the infarcted areas were involved." However, even by the most painstaking and time-consuming dissection, only the major branches of the coronary arteries can be opened and inspected. After performing such a dissection on the uninjected arteries and with our attention focused on the left coronary artery, we have never felt sure that no branches have been missed. Saphir and his associates[1] abandoned attempts to inject the vessels because of the possibility of dislodging or losing a thrombus. By carrying out the injection slowly and carefully and by keeping the injection pressure within physiologic limits (150 mm. Hg), we hoped to minimize this danger. In our preliminary experiments we injected hot agar, tinted with methylene blue. After such a procedure the agar quickly hardened, the injected vessels were distended, their intimas were tinted, and the dissection was much facilitated. Even after this preliminary injection of colored agar, however, the dissection could not be carried out to small vessels obviously injected and tinted.

In some of our earlier experiments the colored agar injected into the left coronary artery returned through the open right coronary artery, thus crudely demonstrating a connection between the two coronaries. Similar observations were made by Oberhelman and Le Count,[2] who injected mercury at a pressure of 150 mm. Hg. It soon became obvious that to untangle the inconsistencies encountered in connection with occlusions of the branches of the left coronary artery, it would be necessary to use a method capable of completely and simultaneously visualizing the entire coronary artery tree in a manner such that the whole course of each individual arterial branch could be studied for defects, narrowing, occlusions, or anastomoses. Karsner[3] called attention to the inadequacy of the available methods for this purpose.

In modern times three types of procedures stand out as having yielded the most information in the hands of different workers. These are all modifications of methods used by numerous previous investigators. The monographs of Gross,[4] of Spalteholz,[5] and of Whitten[6] give an adequate and complete review of the literature of the various methods previously used.

Gross[4] injected the coronary arteries with a suspension of barium sulfate in warm gelatin, fixed the heart *in toto* in formalin, and took stereoscopic roentgenograms. Because of the overlapping of the vessels from the various planes of the heart, interpretation of such films is very difficult. Even the stereoscopic view of such films leaves one much in doubt about anastomotic channels. Because of its crescentic shape, this

is especially true of the vessels of the interventricular septum. On the other hand, occluded branches can be very easily overlooked. In an attempt to overcome these difficulties, Gross and Kugel[7] have recently modified the original method by slicing the injected and fixed heart and then taking stereoscopic roentgenograms of the slices.

Spalteholz,[5] after injecting the coronary arteries with gelatin in which were suspended various minerals or other opaque substances, fixed and bleached the entire heart and then cleared the specimen by a technic similar to that used for clearing small blocks of tissue for microscopic sections. The main objection to this method, as Spalteholz himself recognized, is that the clearing is often irregular and incomplete, especially in the thicker portions of the specimen. Thus one cannot be assured that in every heart he will be able to visualize in its entirety even that part of the coronary artery tree which has been injected. It is obvious that such a method is unsuitable for a complete study of the distribution of all occlusions and anastomoses in individual hearts.

Whitten,[6] after a careful and exhaustive review of the various methods which have been used for exploring the entire vascular system of the heart, concluded that celloidin injection followed by corrosion was the most suitable. However, such a method destroys the tissue completely, and can be used only when no other studies are to be made on the heart. Most of the human hearts obtained at autopsy are too valuable to be almost completely sacrificed to one purpose. This is especially true when infarcts or other lesions are present.

The fact that one must trace a particular vessel through a maze of branches of other vessels is a disadvantage common to all these methods. This has been compared by Crainicianu[8] to a winter scene of a street lined on either side with trees with their bare branches overlapping. Anastomoses between two trees are always apparent, although one knows it cannot be true. If this overlapping could be eliminated, the method of Gross would probably be most suitable for our purpose. Others (Crainicianu,[8] Campbell,[9] and Gross and Kugel[7]), recognizing the limitations of the original method, have attempted to circumvent them by dissecting out various parts of the heart, after injection and fixation, in order to obtain unobstructed roentgenologic views of selected regions for study of particular vessels. None has succeeded in displaying simultaneously all the major vessels and possible anastomotic channels without overlapping.

Spalteholz,[5] using the data of Bianchi, devised a very useful diagram (Fig. 1) illustrating how the coronary arteries would be arranged if they could all be laid out in one plane. If, instead of making a diagram, it were actually possible to do this with each individual heart, our purpose could be accomplished. Spalteholz's diagram was made in much the same manner as a map of the earth is prepared. The conical projection method of cartography consists of the projection of a hemisphere on a hollow

cone. This cone is then cut along one of its meridians, from base to apex, and its conical surface laid out flat. Since the ventricles of the heart make a roughly conical mass and since most of the large vessels lie

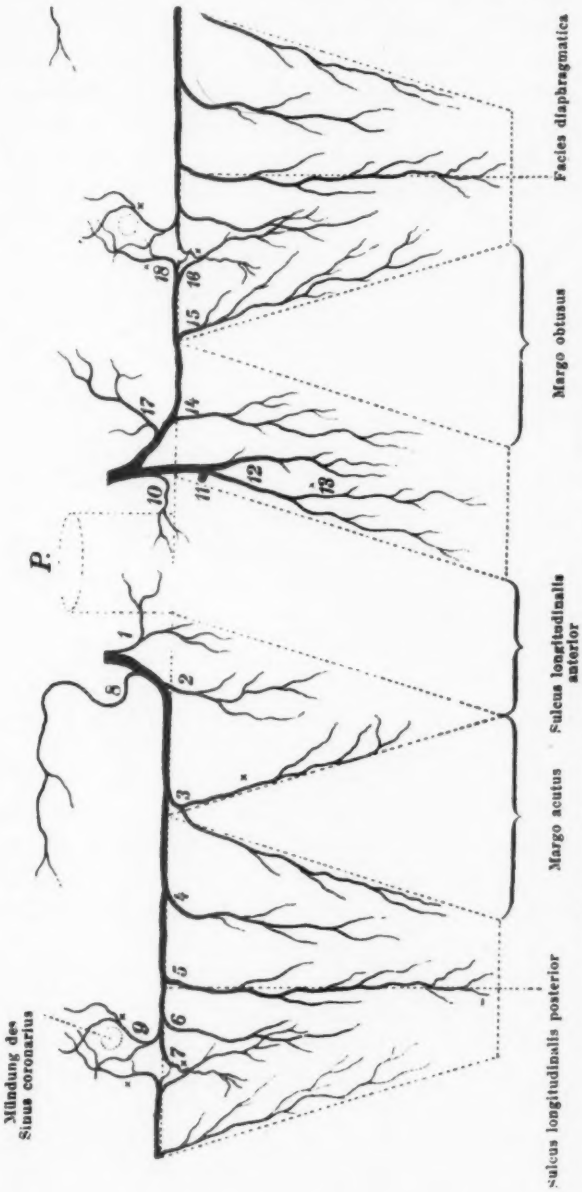

Fig. 1.—Spaltehotz's diagram of the human coronary artery tree

Branches of A. coronaria dextra:

1, A. adiposa dextra
2, R. ventriculi dextri anterior
3, R. marginis acuti
4, R. ventriculi dextri posterior
5, R. sulci longitudinalis posterioris

Branches of A. coronaria sinistra:

6, R. ventriculi sinistri posterior
7, R. ventriculi sinistri posterior accessorius
8, R. atrialis dexter anterior
9, R. atrialis sinister posterior.

Branches of A. coronaria sinistra:

10, A. adiposa sinistra
11, A. septi ventriculorum
12, R. collateralis descendens anterior primus
13, R. collateralis descendens anterior secundus
14, R. ventriculi sinistri anterior
15, R. marginis obtusi
16, R. ventriculi sinistri posterior
17, R. atrialis sinister anterior with R. auricularis
18, R. atrialis sinister posterior.

(From Spaltehotz, W.: Die Arterien der Herzwand, Berlin, S. Heizel.)

close to the surface of this cone, such a procedure should be applicable to the heart. Many apparently formidable difficulties must be surmounted, however, before this simple concept can be transferred to actual practice.

In the first place, the conical mass of the ventricles is vertically transected by the interventricular septum, which lies in another conical plane. This septum carries important arterial branches whose relations to the rest of the coronary tree must be preserved. The original Spalteholz diagram and modifications of it (Saphir and his associates[1]) make no attempt to include the vessels of the interventricular septum. This deficiency is indicated by the inclusion of a cutoff stump of a branch of the left descending coronary artery, which is labelled A. septi ventriculorum. This implies that the septum is entirely supplied by the left descending coronary artery, which is decidedly at variance with the observations of other investigators.

The second question was the selection of the proper meridian on which to cut the ventricular cone to give the least distortion of the picture. This incision should neither transect any large branches with their areas of occlusion nor pass through any of the common areas of possible anastomosis. Spalteholz, in his diagram, recognized this difficulty, for he duplicated a portion of the termination of both coronary arteries. Thus, he suggests cutting on a meridian corresponding to either the acute or the obtuse margin of the heart. However, the former incision would cut through the right coronary artery and the latter through the left circumflex artery. We avoided both these anatomic landmarks and cut on a meridian slightly to the right of the anterior interventricular sulcus. This is a relatively "silent area" in the heart in relation both to large vessels and anastomotic channels.

The third major difficulty is presented by the complicated pattern of valves and valve rings forming the base of the hypothetical ventricular cone (Fig. 9). Furthermore, superimposed on the base of this cone are two irregularly shaped auricles which it is also desirable to preserve. In the midst of these structures are the origins of the two coronary arteries. The position of these latter openings also influenced us in the selection of the proper meridian for our first incision. The meridian selected, when continued across the base of the cone, falls between these two openings, so that when the cone is entirely flattened out, the origins of the two coronary arteries are located at the extreme ends of the straightened out base of the cone, instead of in the middle, as in the Spalteholz diagram. It was also necessary to devise appropriate incisions to divide the auriculoventricular valves and the auricles so that these and the other important structures in the base of the heart would be left in suitable condition for the demonstration of any pathologic changes which might be present.

The success of a method involving such an unrolling of the heart with subsequent roentgenologic visualization of the previously injected arteries would depend largely upon the selection of the proper injection mass. This mass must not be intrinsically injurious to the tissues. It should be freely fluid at a temperature not injurious to the tissues. It should

have sufficient radiopacity to allow visualization of the smallest vessels injected. It should preferably penetrate uniformly to all the smallest arterioles, but not to the capillaries. It should be of such a nature that the injection may be completed rapidly. It should be possible to harden the mass permanently and rapidly after injecting it, so that none could escape during the unrolling process. After hardening the mass, it should be flexible enough so that the heart could be unrolled without distortion. To obviate the danger of producing artifactitious occlusions where none exist, it should contain no large particles. After hardening, it should be of such a consistency that it may be removed easily during the dissection of the coronary arteries. The agar solution used for our preliminary studies seemed ideally adapted to this purpose, if the proper radiopaque substance could be incorporated with it.

From the large number of radiopaque substances available, we selected a lead salt. It was to be expected that lead, with its high atomic weight, would give a dense shadow in vessels so small that only a thin line of the injection mass could enter. A variety of soluble and insoluble lead salts was tested. Many methods of incorporating the lead salt with the agar were tried with varying success. A satisfactory lead-agar mass was finally obtained by dissolving powdered agar in a suspension of freshly precipitated lead phosphate which had never been allowed to dry. This mass was used throughout the series of injections herein reported. To facilitate outlining the distribution of the two coronary arteries, we added methylene blue to the mass injected into the left coronary artery and basic fuchsin to the mass going into the right coronary artery.

Below are given the specific procedures, with their pitfalls indicated, for preparation of the mass, for injection of the arteries, and for unrolling the heart preliminary to making the roentgenogram. After these procedures are carried out, we always perform a complete dissection of the injected arteries in order to confirm, correct, and extend the observations recorded roentgenologically.

TECHNIQUE OF PREPARING HEARTS

Preparation of Tinted Radiopaque Injection Mass

Solution A

Lead Acetate ($Pb(C_2H_3O_2)_2 \cdot 3H_2O$), C.P. ---------- 60.0 gm.
Distilled water ---------- 172.0 c.c.
Heat to dissolve; filter through paper; and allow to cool.

Solution B

Disodium phosphate (Na_2HPO_4 · anhydrous) C.P. ---------- 24.0 gm.
Distilled water ---------- 190.0 c.c.
Heat to dissolve, filter through paper, and allow to cool.

1. Place 1.5 gm. of agar-agar (Difco granular) in a 2,000 c.c. bulb flask.
2. Add 100 c.c. of solution A (lead acetate).
3. Add 1 c.c. of 0.06 per cent phenol red.
4. Add 70 c.c. of solution B (disodium phosphate).

5. Add, from a pipette, 10 per cent NaOH to first permanent pink tinge (about 21 c.c.).
6. Bring total volume to 200 c.c. with distilled water.
7. Boil over free flame with constant stirring until agar dissolves—about ten minutes.
8. Add methylene blue or basic fuchsin in a saturated alcoholic solution—8 c.c.
9. Heat on a free flame for one minute with stirring.
10. Strain, while hot, through several layers of gauze.
11. Distribute into 50 c.c. centrifuge tubes, 35 c.c. to a tube.
12. Stopper and preserve at room temperature.

Final Composition of Injection Mass

Lead (as the insoluble phosphate)	8.00%
Agar-agar	0.75%
Neutral sodium acetate—phosphate buffer	15.00%
Methylene blue or basic fuchsin (in saturated alcoholic solution)	3.00%

In this mass there is a slight excess of phosphate ion, which insures complete precipitation of the lead. If any soluble lead acetate were present, it would diffuse out of the vessels and produce distortion in the roentgenogram. Attempts to dissolve the agar in the autoclave always resulted in a lumpy mass. The solution over a free flame is carried out in a relatively large flask because at first there is much frothing. As the agar dissolves, the frothing diminishes and finally practically ceases when the solution is complete. If the mass is to be kept in stock for any length of time, it is better to add the dyes after it has been remelted for use, just before injecting it into the arteries. The phosphate mixture is so adjusted that the final reaction of the mass is neutral. This is least injurious to the tissues. The insoluble lead phosphate precipitate falls out of suspension so slowly as not to interfere with the injection procedure.

METHOD OF INJECTING ARTERIES

The coronary arteries are injected as soon as possible after the autopsy. We have injected hearts within an hour or two after death, and after they had been kept in the icebox for several days, and have not noted any consistent difference in the ease or completeness of the injection, or any other variation depending upon the length of this interval. We have never found it necessary to relax the vessels by perfusing them with a solution of potassium sulfocyanide, as suggested by Gross,[4] when one wishes to hurry the injection. When necessary, the entire procedure can be completed quite rapidly, that is, within one-half hour. We have repeatedly demonstrated the wet roentgenogram and the completely dissected heart at the autopsy table before the remainder of the autopsy was completed. The details of the injection procedure are as follows:

1. Cannulate the right and left coronary arteries.
   Dissect carefully around either artery just as it leaves the aorta, and tie the cannula in securely, making sure that no branch is proximal to the tie.
2. Warm heart to 44° C. in a bath of physiologic salt solution.
   a. This bath is readily prepared by mixing one part of filtered 18.0 per cent NaCl with 19 parts of warm tap water.
   b. A thermometer should be placed directly in the chamber of the left ventricle, as this is the slowest to warm up. This takes from ten to twenty minutes. This bath is easily kept at the proper temperature (44-45° C.) throughout the injection by means of an immersed electric heating coil and a bimetalic immersion thermoregulator.

3. Simultaneously wash both coronary arteries with about 100 c.c. of warm physiologic salt solution injected at 150 mm. Hg pressure.
   a. The cannulae to the arteries are previously connected to containers (50 c.c. centrifuge tubes) filled with warm physiologic salt solution from the bath. These containers and the rubber tubes connecting them with the cannulae are immersed in the same 44-45° C. bath as the heart.
   b. Each container is connected to a separate mercury manometer, and, by means of Y-tubes, both to the same 50 c.c. syringe, which is used as a source of pressure.
   c. Air bubbles are seen to rise from the heart as the warm salt solution fills the vascular system. The salt solution wash should not be discontinued until no more bubbles rise.
4. Simultaneously inject both coronary arteries with the warm lead-agar mass at 150 mm. Hg pressure.
   a. The mass, kept in 50 c.c. centrifuge tubes, is previously melted in a separate bath of boiling water.

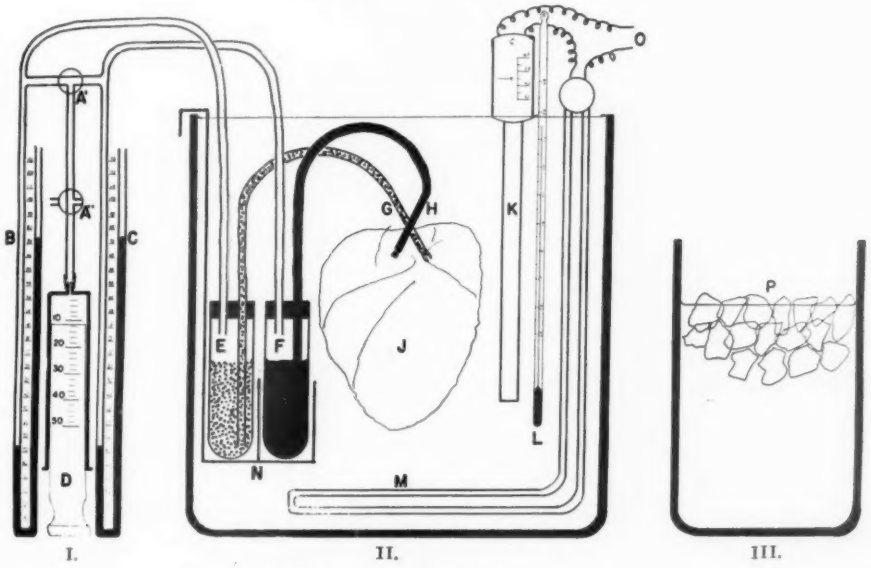

Fig. 2.—Apparatus for injection, composed of:

I. Double manometer consisting of:
A' and *A''*, three-way stopcocks
B, Manometer for left coronary artery
C, Manometer for right coronary artery
D, 50.0 c.c. syringe for pressure.

II. 45° C. salt solution bath containing:
E, Reservoir for injection mass for left coronary artery
F, Reservoir for injection mass for right coronary artery
G, Cannula in left coronary mouth
H, Cannula in right coronary mouth
J, Heart
K, Thermoregulator
L, Thermometer
M, Electric Heating Coil
N, Holder for reservoirs
O, To electric outlet.

III. Cold salt solution bath with:
P, Ice.

   b. The mass after melting is cooled and kept liquid by immersion in the same 44-45° C. bath as the heart.
   c. The injection is continued until the manometer readings remain constant for several minutes at 150 mm. Hg pressure without the application of any more pressure. This usually takes less than five minutes.
5. To insure flow through any anastomoses which may be present, the pressure in the left coronary artery is then reduced to zero or lower, and that in the right

coronary artery kept at 150 mm. Hg. This condition is maintained for several minutes. The process is then reversed, i.e., low pressure maintained in the right coronary artery, and high in the left. (At this stage the heart should be lifted gently from the salt solution for short inspections to be sure that the injection is progressing satisfactorily.)

6. Set the mass by cooling the heart in a separate bath of iced physiologic salt solution.
   a. The cannulae are previously clamped with the pressure at 150 mm. Hg and the heart disconnected.
   b. This bath is readily prepared by mixing one part of filtered 18.0 per cent NaCl with ice and sufficient tap water to make a total volume of 20 parts.

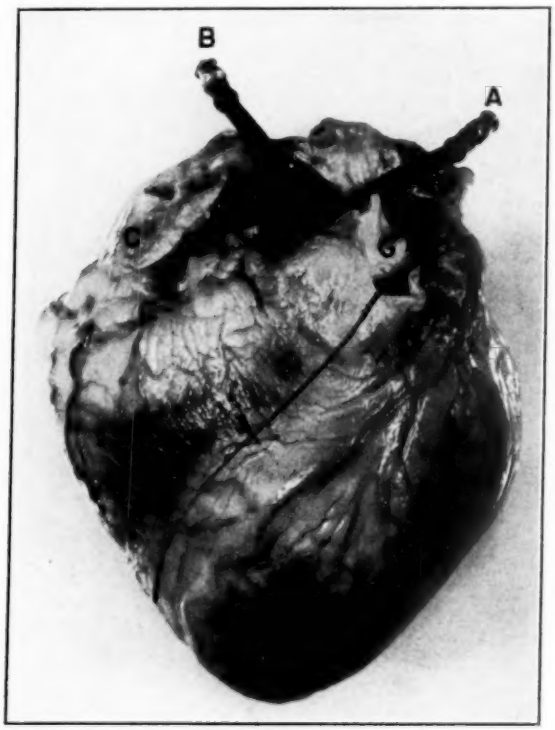

Fig. 3.—Intact heart with incision 1 indicated. (Reduced to ½ normal size.)

In Figs. 3 to 8 the following structures are labelled:

A, Cannula in right coronary orifice
B, Cannula in left coronary orifice
C, Right auricle
D, Left auricle
E, Right ventricle
F, Left ventricle
G, Pulmonary artery
H, Interventricular septum
I, Pulmonary valve
J, Aortic valve
K, Mitral valve
L, Tricuspid valve.

   c. The mass sets quickly at temperatures below 20° C.
   d. The mass will remain solid at room temperature.
7. Dissect the heart to flatten out the coronary arteries (*see* method and steps below).
8. Make roentgenogram of flattened-out coronary arteries.
   a. Place the heart with the pericardial surface in contact with the x-ray film holder.
   b. Technical factors used in making radiographs of the unrolled heart:

Tube—XP—1—W; fine focus; distance, 42 inches; milliamperes 20; kilovolts 48; medium cone; time, 1 second; plain folder.

9. Open the coronary arteries as far as possible.
   a. The injection mass will be a gray mush, easily removed in small bits.
   b. The intima of the vessels will be tinted red if reached by the mass from the right coronary cannula, blue if reached by that from the left, and purple if reached by both.

The apparatus for injection is shown in Fig. 2. The entire apparatus is compact, occupying a space 28 inches long and 15 inches wide. It can, if necessary, be constructed from equipment ordinarily at hand.*

INCISIONS AND STEPS NECESSARY TO UNROLL THE HEART AND FLATTEN OUT THE CORONARY ARTERIES

First Incision (Fig. 3). Starting in the pulmonary artery, opening up the pulmonary valve and right ventricle on a line just to the right of the anterior interventricular sulcus, and extending completely to the apex.

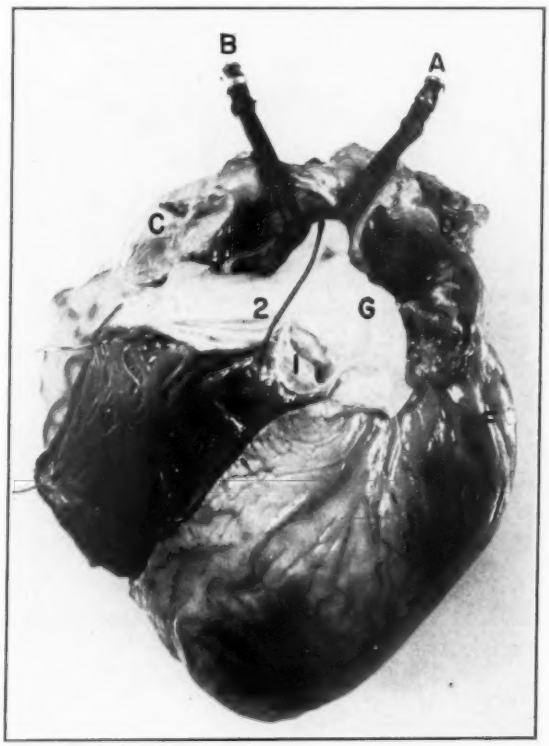

Fig. 4.—Incision 1 has been made, and incision 2 is indicated. (Reduced to ½ normal size.)

Second Incision (Fig. 4). Starting in the aorta, between the right and the left anterior cusps of the aortic valve, behind each of which is one of the cannulated coronary artery orifices, extending down about 1 cm. into the base of the septum, and thus dividing again the pulmonary valve and its ring.

*The entire constant temperature apparatus, including thermoregulator, immersion coil, and bath, may be obtained from the American Instrument Company, Baltimore, Md.

The holders for the injection mass were made by Mr. P. Tuzik, 82 Chikatawbut Street, Dorchester, Mass.

The double manometer may be obtained from Macalaster Bicknell Co., of 171 Washington Street, Cambridge, Mass.

Third Incision (Fig. 5). Starting at the inferior termination of the second incision, continuing anteriorly along the base of the interventricular septum to the upper end of the anterior border of this septum, and then along the anterior border of this septum, completely to the apex; thus separating the interventricular septum anteriorly from the ventricles.

Fourth Incision (Fig. 6). Starting again at the inferior termination of the second incision, continuing posteriorly along the base of the interventricular septum to the upper end of its posterior border, and then along the posterior border of this septum, completely to the apex; thus connecting with the third incision and completely removing the interventricular septum.

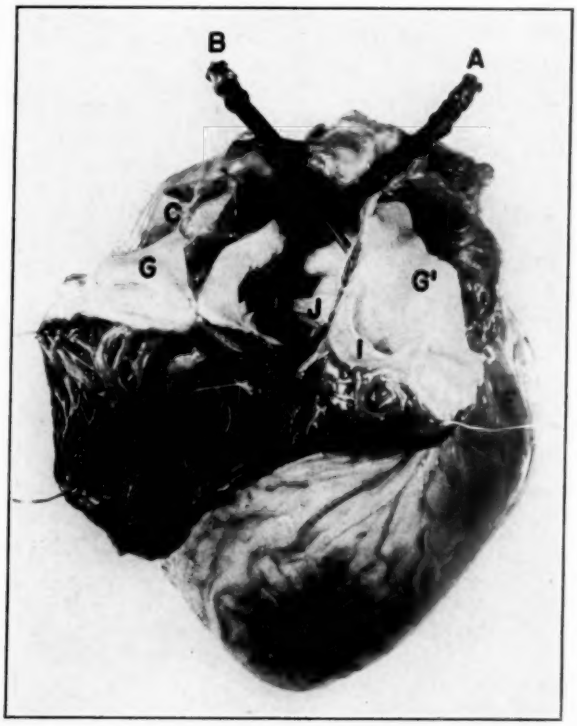

Fig. 5.—Incisions 1 and 2 have been made, and incision 3 is indicated. (Reduced to ½ normal size.)

Fifth Incision (Fig. 6). Starting at the middle of the free border of the anterior cusp of the mitral valve, this cusp is bisected, and the incision continued through the mitral ring, and through the aortic ring to separate the left aortic cusp from the posterior aortic cusp. The left auricle having been entered from below, the incision is carried parallel to the left side of the interauricular septum to and through the pulmonary veins to unroll completely the left side of the heart.

Sixth Incision (Fig. 7). Starting at the junction of the anterior and the medial cusps of the tricuspid valve, dividing the tricuspid ring and continuing across the aortic ring to separate the right anterior aortic cusp from the posterior aortic cusp. The right auricle having been entered from below, this incision is carried parallel to the right side of the interauricular septum, to and through the superior vena caval opening to completely unroll the heart.* (Fig. 8.)

*The roentgenogram of the vessels of this heart is shown in Fig. 12.

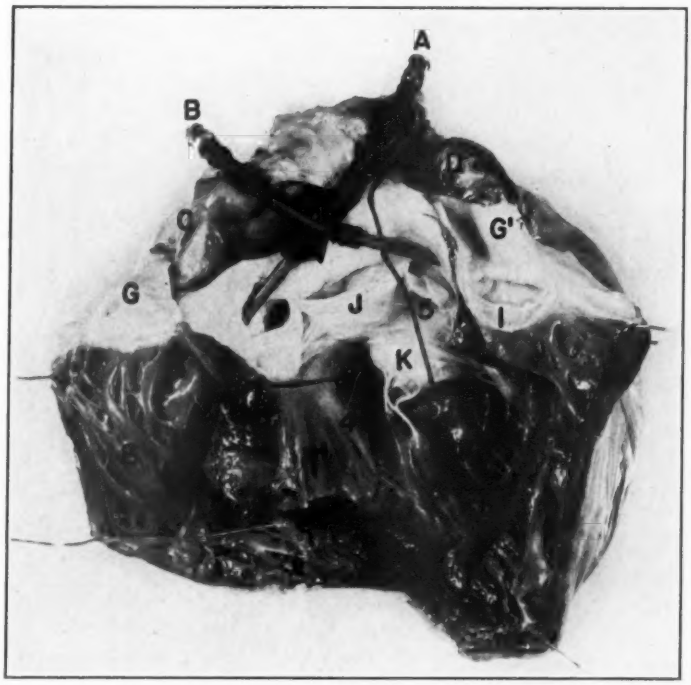

Fig. 6.—Incisions 1, 2, and 3 have been made, and incisions 4 and 5 are indicated. (Reduced to ½ normal size.)

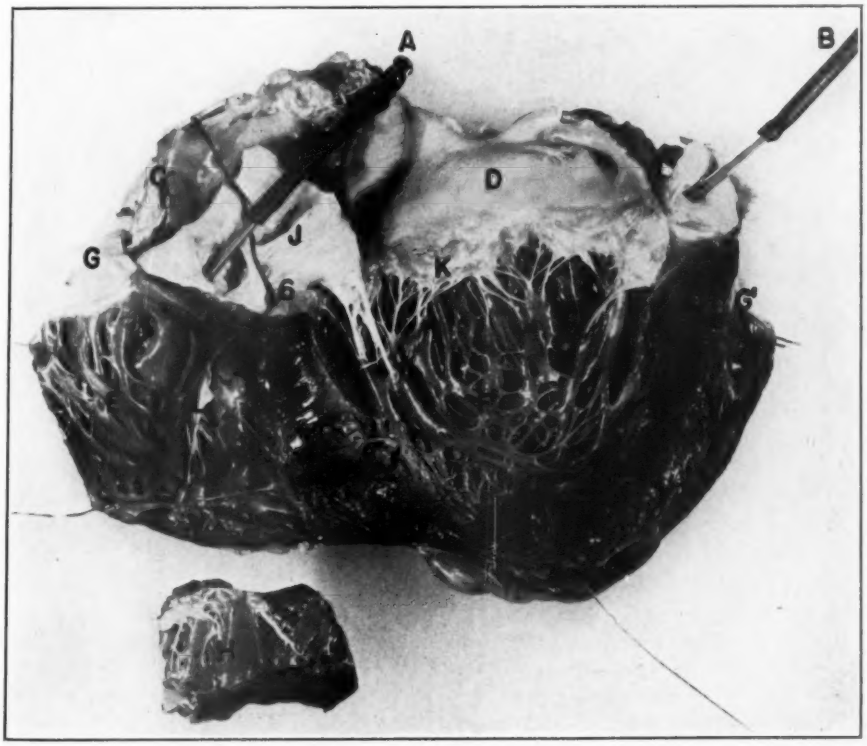

Fig. 7.—Incisions 1, 2, 3, 4, and 5 have been made and incision 6 is indicated. (Reduced to ½ normal size.)

Particular attention is called to incisions 3 and 4, which were devised to remove the interventricular septum. It is often more convenient to make incision 4 before incision 3. The object of these two incisions is to remove completely the interventricular septum from the remainder of the heart. This is accomplished by whatever complicated incisions are found necessary in each particular case, following,

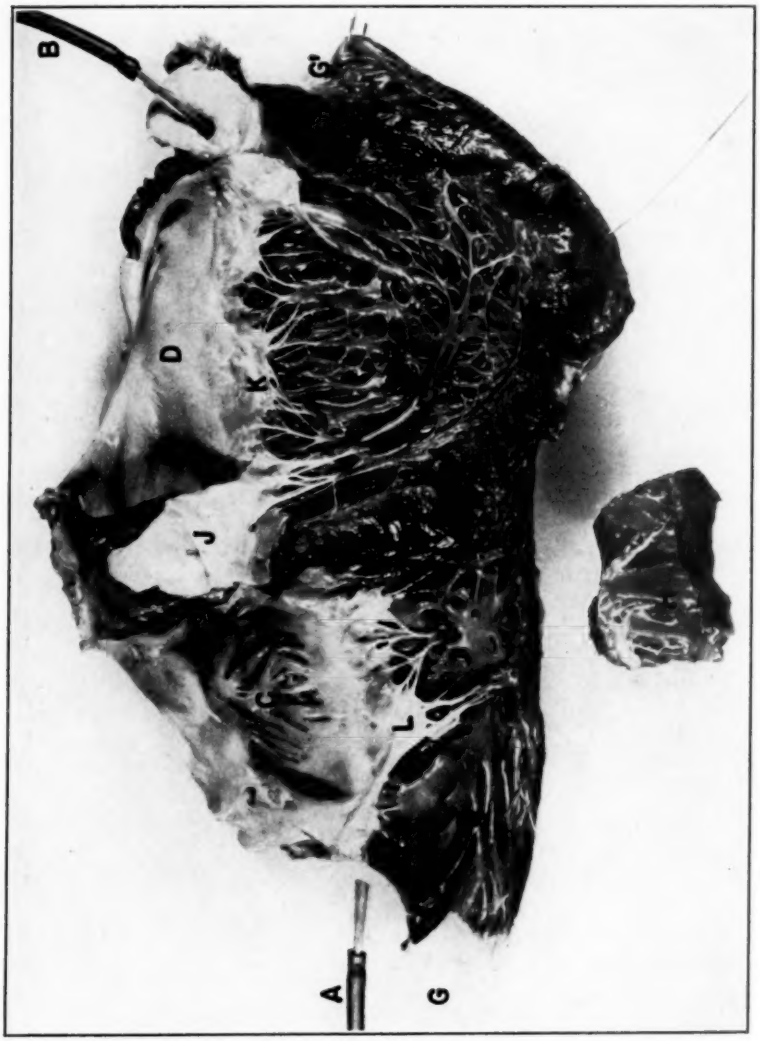

Fig. 8.—Completely unrolled heart viewed from the endocardial surface. (Reduced to ½ normal size.)

however, the landmarks noted above. For these two incisions a small sharp scalpel is most convenient, all the other incisions being made with scissors.

In Fig. 9, from Cunningham,[10] the positions of incisions 1, 2, 5, and 6 are indicated on a diagram of the valves and valve rings of the heart. From this it can be seen that the pulmonary valve is cut in two pieces, and the aortic valve in three segments, by this series of incisions. The auriculoventricular valves are cut across only once. If during the course of the dissection a lesion of the heart which it is undesirable to cut through is encountered, it is always easy to turn aside slightly without altering the general plan significantly.

TECHNIQUE OF STUDYING INJECTED HEARTS

Comparison of Intact and Unrolled Heart

The completeness with which this kind of dissection eliminates the confusing overlapping of arterial shadows obtained by Gross' method is illustrated by comparing Figs. 10 and 11. These pictures were made from the same injected heart* before and after carrying out such a dissection. In Fig. 10, the vessels of the intact heart are viewed as if seen from the back, as in Gross' monograph.[4] In Fig. 11, the unrolled heart, these vessels are viewed as if seen from the pericardial surface. The picture in this particular heart resembled the Spalteholz diagram so closely that it was possible to label the arteries exactly as they are labeled on that diagram. Only by comparison of the two pictures was it possible

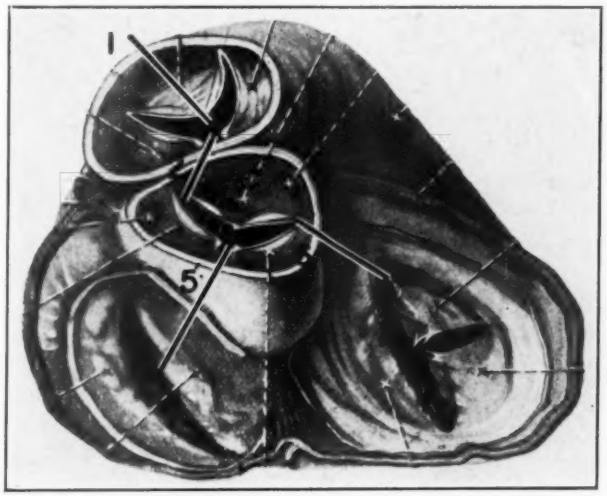

Fig. 9.—Base of ventricles with valves:
1, Incision 1 from pericardium to pulmonary valve
2, Incision 2 from pulmonary to aortic valve
5, Incision 5 from aortic to mitral valve
6, Incision 6 from aortic to tricuspid valve.
(From Cunningham's Text-Book of Anatomy, William Wood & Company.)

to label the same vessels in Fig. 10 of the intact heart. Then, to make correlation easier, the key numbers were placed as far as possible in the same relative positions near the appropriate vessels in both figures. Also, the fact that in both figures the branches of the left coronary artery are tinted blue, and the branches of the right coronary artery red aids in the correlation.

Since at no place in the roentgenogram of the dissected heart is the shadow of more than a single thickness of the cardiac wall present, many soft tissue details can also be seen. However, since the injection mass

*This heart (Case 24) was hypertrophied (600 gm.) and was the seat of aortic stenosis with calcification of the aortic ring and leaflets. This calcification is seen in the roentgenogram just above the mouths of the coronaries.
This picture also shows considerable arteriosclerosis of the various arterial branches with some distortion of their lumina and some calcification.

used does not penetrate vessels of the caliber of those going to the valves, this method gives no information about the vascularization of the valves. In pictures such as Fig. 11 each individual vessel can be studied throughout for points of narrowing due to arteriosclerosis. Complete occlusions, of course, are easily seen and localized. The question of anastomosis can also be adequately studied.

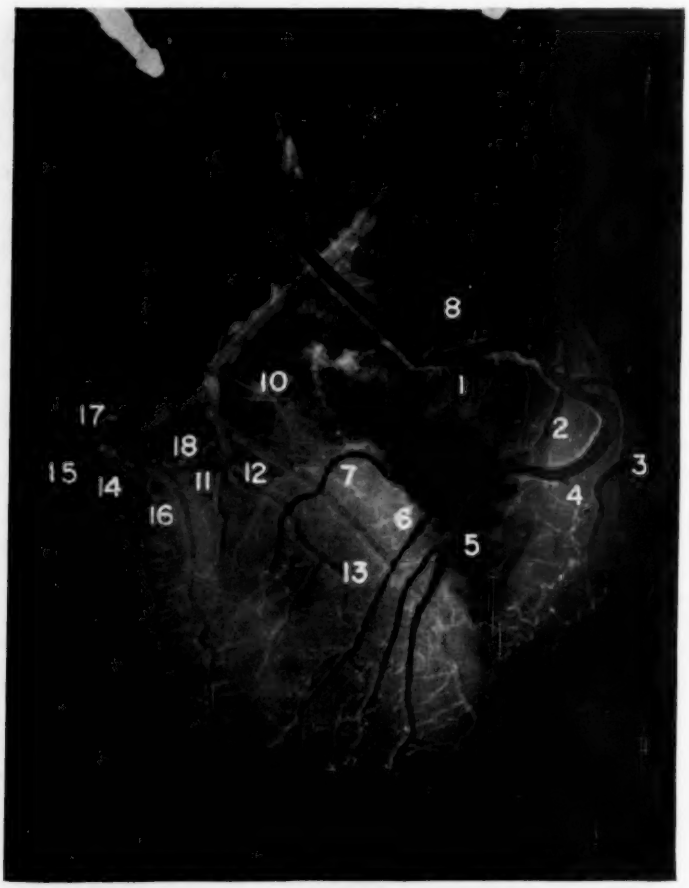

Fig. 10.—Case 24, Intact heart. Numbering of vessels same as in Figs. 1 and 11. (Reduced to ⅔ normal size.)

Appearances of Arteriosclerotic Narrowing and Occlusion in Injected Vessels

The contour of the shadow of the injected normal arteries is that of a band with smooth walls (Fig. 12). The tapering is uniform. The course of even the most tortuous vessels is easily followed. The occasional overlapping of large vessels causes no confusion. The diameters of each vessel and its branches can be easily measured. Because the exposure is made with the pericardial surface in contact with the film holder, the roentgenogram shows almost no distortion of the diameter of the larger,

more superficial vessels. The diameter of the smaller, penetrating vessels is, if anything, slightly enlarged, making them easier to follow.

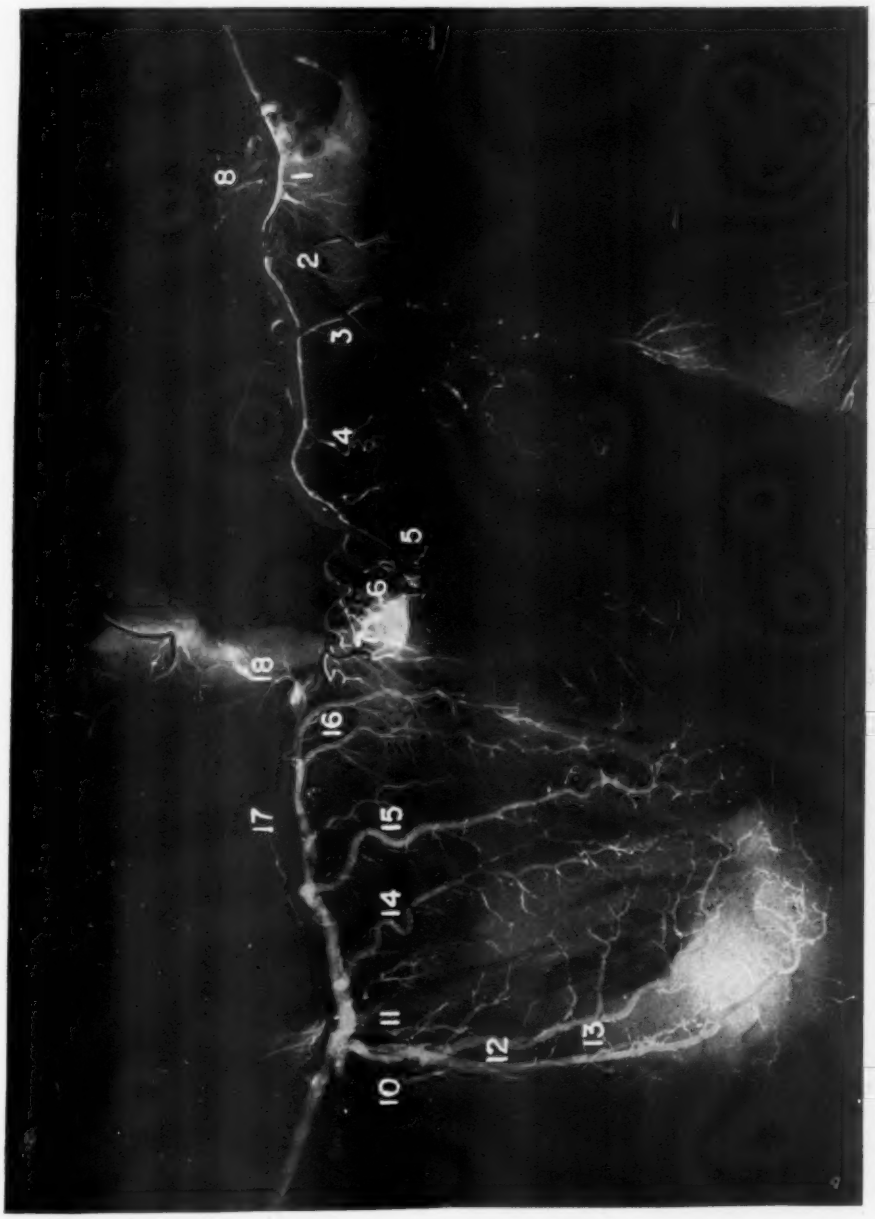

Fig. 11.—Case 24. Unrolled heart. Numbering of vessels same as in Figs. 1 and 10. (Reduced to ⅝ normal size.)

Arteriosclerotic plaques which narrow or distort the lumen are easily seen as irregularities in the contour of the shadow. Not all such plaques cause a narrowing of the lumen. Some cause a distortion of contour without narrowing (Fig. 14). Others cause no distortion whatsoever and are not detected until the arteries are opened up. Stewart, Birchwood,

and Wells,[11] using a method similar to that of Gross and injecting at a pressure of 95 mm. Hg, reported that most arterioselerotic plaques in the coronary arteries cause no narrowing of the lumen. We have repeatedly found irregularities at the sites of arteriosclerotic plaques in the coronaries (Fig. 13, left circumflex artery, and Fig. 16, left descending artery), in spite of the fact that our roentgenograms were taken while maintaining an even higher internal pressure (150 mm. Hg). This discrepancy is probably due to the fact that unrolling the heart produces a sharper, less distorted view of the injected vessels and brings out details better.

Calcified plaques present a picture interesting in its variations. If the radiopacity of the plaque is the same as that of the injection mass, the shadow of the plaque may fuse with that of the column representing the lumen, or may appear as an outpocketing of this lumen (Fig. 14, left descending artery.) When the lead-agar and the calcified plaque are of different densities, the plaque often stands out quite distinctly (Fig. 15, right coronary artery.) Interesting pictures are obtained when a row of small plaques in the wall of the artery are separated from the lumen by a noncalcified layer. Then the shadow of the lead-agar in the lumen has a wavy irregular contour, next to which, and parallel to which, is a series of irregular opaque blotches representing the calcified plaques (Fig. 13, right coronary artery.)

Zones of complete occlusion usually appear as obvious defects in the shadow of the injected lumen. However, if the occluded zone is calcified, the shadow of this calcium may simulate injection mass in the lumen. No final decision as to the patency or occlusion of any vessel can be made from the roentgenogram alone. This decision is always reserved until after the coronary arteries have been dissected.

Anastomotic Zones Between Right and Left Coronary Arteries

In the roentgenogram of the unrolled heart the possible anastomotic zones between the right and left coronary arteries are all widely separated, whereas in that of the intact heart these zones directly overlie one another. The first of these zones lies in the anterior portion of the right ventricle just to the right of, and parallel to, the anterior interventricular groove. The first incision described above is made near this zone. Along this line are the terminal twigs of many of the branches of the right coronary artery, and also such branches of the left descending coronary artery as may go to the right ventricle. These vessels are quite obvious before dissection because the branches of the right and left coronary arteries are injected with masses of different colors. One can avoid going directly through this zone by placing the incision properly. In Fig. 11, along the cut edge of the heart, parallel to the left descending coronary artery, several terminal twigs of the right coronary artery may be seen. If there were any injected anastomotic vessels bridging this gap, their shadows would be perfectly obvious.

The second possible zone of anastomosis between the right and left coronary arteries lies in the region of the posterior interventricular groove. According to Spalteholz,[5] in 80 per cent of human hearts the posterior descending artery, lying in this groove, is the terminal portion of the right coronary artery. This is exemplified by the heart shown in Fig. 11. Ordinarily branches, or at least terminal twigs, from both the left circumflex coronary artery and the left descending artery reach this groove. We have found, as have Spalteholz,[5] Whitten,[12] and others, that the commonest variations in the vascular supply of the heart are found in this zone. These variations are especially easy to study in the roentgenograms of the unrolled heart and will be the subject of a separate communication. It is in this region that deceptive shadows of seemingly anastomotic channels are most often encountered in the roentgenograms; individual branches of fair caliber often appear to bridge this gap between the left and the right coronary arteries. On dissection, however, these vessels are found to lie in different planes.

In both Saphir's modification[1] of Spalteholz's diagram and a drawing in *Cunningham's Textbook of Anatomy* (Fig. 9), a large artery is shown as a normal anastomotic channel between the termination of the left circumflex coronary artery and the right coronary artery. Mautz and Gregg[13] experimentally induced the formation of a large anastomotic channel in this location in a dog by tying off the right coronary artery. In the human heart we have only once (Case 34, Table I) found such a channel. Our dissections have convinced us that in man such roentgenographic appearances should be considered as artifacts unless their existence is confirmed by dissection.

The interventricular septum provides the third possible zone of anastomosis between the right and the left coronary arteries. One or more large branches of the left descending coronary artery regularly penetrate this structure. It also ordinarily receives a larger number of smaller branches from its posterior border. These branches of posterior origin vary in their source, depending upon which vessels traverse the posterior interventricular groove. These may be branches either of the right or left coronary artery, or both. After injecting the heart and before making the roentgenogram, we remove this septum and turn it so that its left ventricular surface is in contact with the x-ray folder, thus avoiding overlapping of vessels. Fig. 11 not only shows the stump of the septal arteries, as in Spalteholz's diagram, but also their complete distribution in the body of the septum. This is even better shown in Figs. 12 and 16.

Method of Proving the Presence of Anastomoses

A final decision as to the presence or absence of an anastomosis would often be impossible if we had to depend upon the roentgenogram alone, or even upon the roentgenogram and ordinary dissection. The use of dyes of different colors in the masses used to inject the right and left

coronary arteries is all-important. When the injection, roentgenogram, and dissection of the vessels are completed, the distribution of these dyes enables one to say with certainty from which coronary opening a particular vessel was injected. Three types of anastomoses are then recognizable.

The anastomotic channels may carry the blood from one large branch of one of the two coronary arteries to another large branch of the same vessel, or serve to bridge a gap in one of the branches of the vessel. We have called these left to left (L to L), or right to right (R to R) anastomoses. An obvious R to R (or L to L) anastomosis is present when there is a definitely occluded zone in the lumen of one of the coronary branches, and the distal part of this branch is fully injected with mass of the same color as that found proximal to the zone of occlusion. This is the commonest type of anastomosis (Fig. 16). In the absence of a point of occlusion with injection beyond, all the precautions enumerated will not exclude the presence of functional anastomotic channels between branches of the same coronary artery. Since the procedure used yields adequate objective evidence of all other types of anastomoses, this might have proved a serious defect of the method. However, anastomoses of this kind were detected by tying off one or more of the smaller arterial branches just before injection (Fig. 13). The injected mass was thus prevented from penetrating beyond the artificial occlusion except via anastomotic channels. This special procedure is not necessary in every case but was employed often enough to rule out the possibility that anastomoses of this kind occur in normal hearts.

There is a second type of anastomosis, in which, proximal to a completely occluded point, is found mass of one color filling the vessel and its branches, whereas distal to the occlusion, in what is obviously the continuation of the same vessel, is found mass of the opposite color. We have called these left to right (L to R) or right to left (R to L) anastomoses. Under such circumstances, it is obvious that a portion of the myocardium and of the vessels supplying it have become entirely dependent upon the opposite coronary artery for their blood supply (Fig. 14).

A third form of anastomosis is that in which one or more arterial branches receive blood from both coronary arteries. A vessel which receives blue mass from the left coronary artery, and red from the right, necessarily stains purple (Fig. 15), and we have called this a convergent anastomosis. On rare occasions all the branches of both coronary arteries are tinted purple of varying shades. More often a few branches distal to their occluded zones become purple, whereas other similarly occluded branches are filled with either pure red or pure blue mass.

ANALYSIS OF RESULTS

Fifty-six human hearts have been injected and studied by a uniform technique similar to that described above. In ten of these the injection was imperfect because of technical difficulties. The commonest sources

of error were the use of a salt solution immersion bath which was too cool, or of a leaky or plugged pressure system. Of the remaining 46 hearts, 8 were from patients less than 50 years of age. Inasmuch as we wished to clarify the relationship between anastomoses and occlu-

TABLE I

COMPLETE DATA ON ALL HEARTS INJECTED

CASE NO.	AGE (YR.)	DEGREE OF CORONARY ARTERIO-SCLEROSIS	ARTERY OCCLUDED	TYPE OF ANASTOMOSIS	IN-FARCT	DEGREE OF HYPER-TENSIVE HYPER-TROPHY	VALVE WITH LESION
1	73	++	R	L to R		+++	AV
2	58	+	R	L to R		++	
3	57	+		Con.		+	
4	64	0					
5	61	+++	LD, LC, R	L to R; L to L			
6	52	+					
7	51	0		Con.			MV
8	72	0					AV
9	62	++	LD	L to L			
10	72	+					
11	53	+++	LD, LC, R	L to L; R to R; L to R; R to L; Con.	*		
12	67	++					
13	62	+					
14	72	0					
15	78	+		R to L			AV, TV, MV
16	76	++					
17	66	+++	LD, LC, R	L to L; L to R		+++	
18	69	+++	LC, R	L to L; L to R; R to R	*		
19	51	+	LC	L to L	*		
20	56	0					
21	62	0					
22	62	+++	LD	Con.	*		
23	65	++	R	L to R; R to L			MV
24	80	+++					AV
25	56	+					
26	58	0					
27	80	++	LC	Con.		++	
28	65	0					AV
29	67	0					
30	63	+					
31	66	+++	LD	L to L			
32	63	+				+	
33	72	+					
34	70	+++	LC, R	L to L; L to R	*		
35	75	+++	R	L to R			
36	63	0					
37	72	+				++	MV
38	55	+++	LD, LC, R	L to L; R to R; Con.	*		

Arteriosclerosis: 0, none; +, slight; ++, moderate, +++, marked.

Artery occluded: *LD*, left descending coronary artery or its branches; *LC*, left circumflex coronary artery or its branches; *R*, right coronary artery or its branches.

Type of Anastomosis: *L to L*, anastomosis between branches of the left coronary artery; *R to R*, anastomosis between branches of right coronary artery; *L to R*, branches of the right coronary artery entirely supplied from the left coronary artery; *R to L*, branches of the left coronary artery entirely supplied from the right coronary artery; *Con.*, branches of one or both coronary arteries supplied by a mixture of blood from both coronary arteries.

Valvular lesion: *TV*, tricuspid valve; *MV*, mitral valve; *AV*, aortic valve.

sions of the coronary arteries, these 8 hearts were purposely omitted, for, according to previous workers in this field, anastomoses are likely not to be well established before the age of 50 years.

The data on these 38 hearts are shown in Table I. Seven (Cases 4, 14, 20, 21, 26, 29, and 36) were essentially normal, and 8 (Cases 6, 10, 12, 13, 16, 25, 30, 33) showed only minimal or moderate degrees of atheromatosis of the coronaries. No anastomoses were present in any of these fifteen hearts. The remaining 23 hearts were definitely pathologic. The lesions, although quite varied, consisted principally of (1) marked arteriosclerosis with or without complete occlusion of coronary artery branches, (2) valvular lesions of various types, and (3) hypertensive hypertrophy; some of the hearts displayed various combinations of these three kinds of abnormalities. Three hearts (Cases 3, 7, 15), although from patients over 50 years old, were also purposely omitted from further consideration at this time. In these three hearts anastomoses without occluded vessels were present. They showed hypertensive hypertrophy, rheumatic mitral stenosis, and subacute bacterial endocarditis respectively. The above omissions reduce the number of hearts under discussion to 35.

In Table II, these 35 hearts are grouped according to age and the presence or absence of anastomoses in the coronary artery tree, and we see that there is a complete lack of correlation between the two. In both groups, with and without anastomoses, over 80 per cent of the hearts were from persons over 60 years of age. Nevertheless, in 57 per cent of

TABLE II

AGE INCIDENCE OF CORONARY ARTERY ANASTOMOSES

	AGE IN DECADES			
	50-59 YR.	60-69 YR.	70-80 YR.	TOTAL
No anastomoses	4	9	7	20
Anastomoses	4	7	4	15

the hearts no coronary artery anastomoses were demonstrable by a standard technique which readily visualized such anastomoses in the remainder. In all 15 hearts in which anastomoses were found, there were also one or more occluded coronary artery branches. No occluded branches were found in the other 20 hearts without anastomoses. Thus it would appear that coronary artery anastomoses are related less to advancing age than to the necessities which arise as a result of occlusion of coronary artery

TABLE III

ARTERIOSCLEROSIS AND CORONARY ARTERY ANASTOMOSES

	DEGREE OF ARTERIOSCLEROSIS				
	NONE	SLIGHT	MODERATE	MARKED	TOTAL
No anastomoses	9	8	2	1	20
Anastomoses	0	2	4	9	15

branches. The occlusions themselves are, of course, in practically all instances, a sequence of arteriosclerosis, and there is in general a definite increase in arteriosclerosis of the coronary arteries with increase in age, but many individual variations are encountered. In a given heart, the more extensive the arteriosclerosis, the greater the probability that coronary artery occlusion will occur. Therefore, there should be a direct correlation between the incidence of anastomoses and the amount of coronary arteriosclerosis. In Table III the hearts are grouped according to the degree of arteriosclerosis and the presence or absence of anastomoses. In preparing these data the amount of arteriosclerosis in the coronary arteries was estimated in four degrees of intensity, namely, none, slight, moderate, and marked. In arriving at this estimate, both the roentgenogram and observations on the dissected coronaries were utilized. In 85 per cent of the hearts that showed no coronary artery anastomoses, there was less than a moderate degree of coronary arteriosclerosis. Of the hearts in which there were coronary artery anastomoses, 80 per cent showed moderate to marked arteriosclerosis.

For the 15 hearts in which there were completely occluded coronary artery branches Table IV summarizes the data as to the sites of the occlusions, the types of anastomoses, and the presence of infarcts. Adequate statistical study of the interrelation of these factors will have to await a larger series. A few significant observations can, however, be made. In the 25 occluded coronary artery branches in these 15 hearts, there is a higher incidence of occlusion of the right coronary artery, or its branches, than of either of the main divisions of the left coronary artery or their branches. Moritz and Beck[14] also found a high incidence of right coronary artery occlusions after the age of 60 years.

TABLE IV

RELATION OF OCCLUDED VESSEL TO ANASTOMOSES PRODUCED

CASE NO.	OCCLUDED VESSEL			INFARCT	NATURE OF ANASTOMOSES				
	LD	LC	R		L TO L	R TO R	L TO R	R TO L	CONVERGENT
1			*				*		
2			*				*		
5	*	*	*		*		*		
9	*				*				
11	*	*	*	*	*	*	*	*	*
17	*	*	*		*		*		
18		*	*	*	*	*	*		
19		*		*	*				
22	*			*					*
23			*				*	*	
27		*							*
31	*				*				
34		*	*	*	*		*		
35			*				*		
38	*	*	*	*	*	*			*
Totals	7	8	10	6	9	3	9	2	4

Abbreviations as in Table I.

In six (Cases 5, 11, 17, 18, 34, 38) of these fifteen hearts there were complete occlusions in branches of more than one of the three major divisions of the coronary arteries. Because of the fairly common occurrence of multiple points of occlusion, impressions of the incidence of occlusions are valueless unless based on a method permitting complete study of all the coronary artery branches in every heart. In four (Cases 11, 18, 34, 38) of these six hearts with multiple complete occlusion, there were either fresh or healed infarcts. However, two infarcts, one fresh and one healed, were also present in each of two other hearts (Cases 19 and 22) in which there was only one completely occluded branch. Thus, with more extensive arteriosclerosis and a large number of vessels affected, the probability of infarction was greater. Infarction, however, may occur in a heart with very little arteriosclerosis and with only one major vessel completely occluded (Case 19).

Analysis of the paths of the anastomotic circulation following complete occlusions brings out the point that in only three hearts (Cases 9, 19, 31) was the compensatory anastomotic circulation entirely dependent upon connection with the coronary artery whose branch was occluded. In all other instances there was an anastomotic channel established with the opposite coronary artery. As a result of this new pathway the branches distal to the occlusion were then either fed entirely from the opposite coronary artery, or were supplied with a mixture of blood from both coronary arteries. In only two instances (Cases 11 and 23) was an occluded branch of the left coronary artery thereafter fed entirely from the right coronary artery. Also, it was unusual for an occluded branch of the right coronary artery to receive its blood supply entirely from that artery after the occlusion occurred. There were only three examples (Cases 11, 18, and 38) of this type of readjustment of the circulation. In nine hearts (Cases 1, 2, 5, 11, 17, 18, 23, 34, 35), however, the left coronary artery had served as the source of supply for an occluded branch of the right coronary artery. It should be noted that in Case 11 examples of all three of these types of anastomoses were found. This heart, however, presented a very complicated anastomotic circulation (Fig. 15). In general, it can be said that blood from the left coronary artery usually reaches whatever branches of either coronary artery which are deprived of their original source of supply. Sometimes this anastomosis from the left coronary artery furnishes the whole supply, but there is often an intermingling with blood coming by anastomotic channels through the right coronary artery.

ILLUSTRATIVE CASES

Almost without exception, the roentgenograms of each of the 56 hearts thus far injected were worthy of individual study and threw light on one or more points in cardiac anatomy or pathology. This was especially true of the injected arteries, but the unrolled heart also gave such a

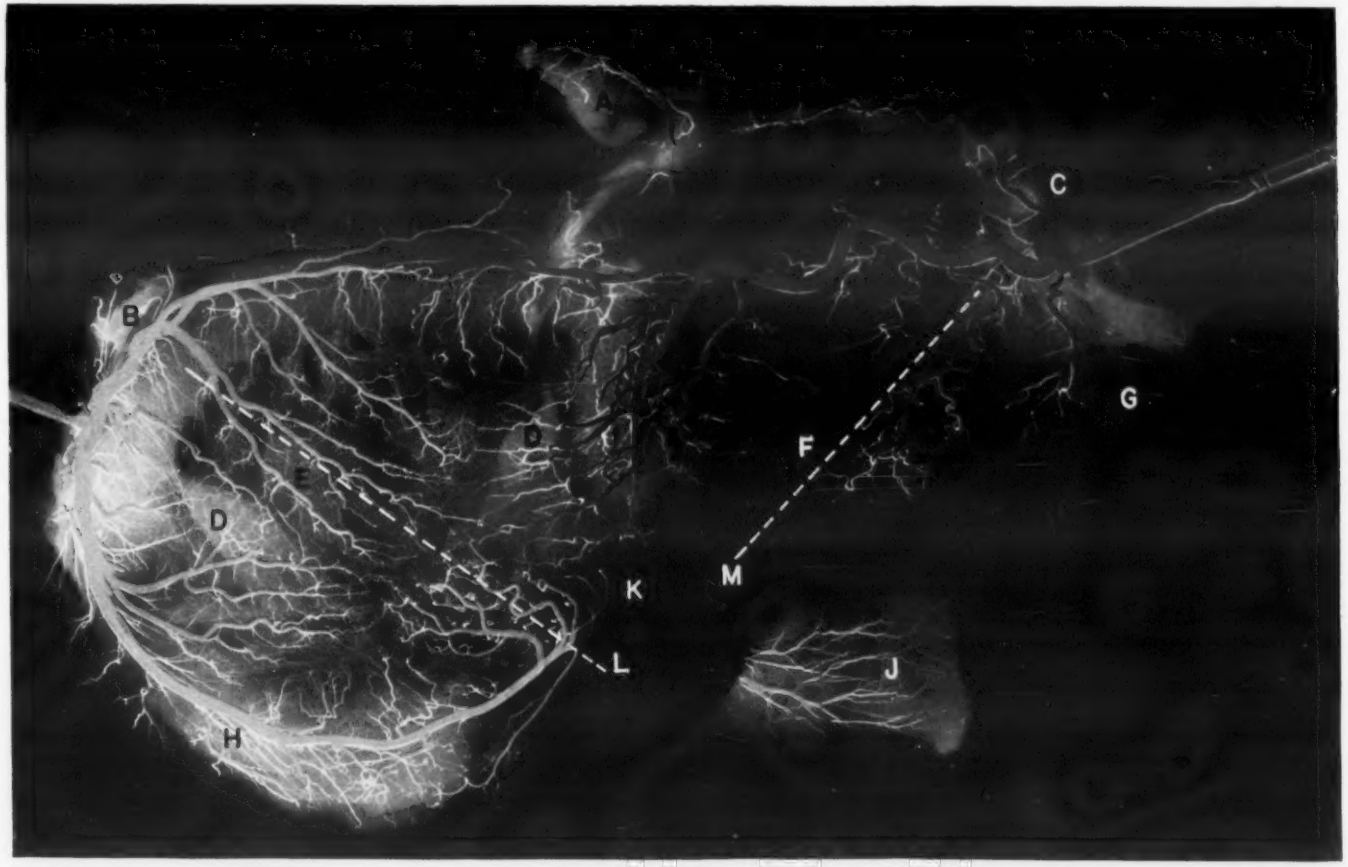

Fig. 12.—Case 32. Normal heart. (Reduced to ⅜ normal size.)

A, Interauricular septum
B, Left auricular appendage
C, Right auricular appendage
D, Left anterior papillary muscle (divided in 2 parts)
E, Left posterior papillary muscle
F, Columnae carneae
G, Conus arteriosus
H, Anterior edge of interventricular septum
I, Posterior edge of interventricular septum
J, Interventricular septum
K, Apex of heart
L, Obtuse border of heart
M, Acute border of heart.

satisfactory soft tissue shadow on the roentgenogram that most of the various intracardiac structures could be identified, studied, measured, and many of their abnormalities recognized. We are reproducing the roentgenograms of only five of our forty-six successfully injected hearts. These five hearts have been selected to illustrate the possibilities of the study of cardiac vascular disease by this method. Only a brief discussion of the clinical history of each patient will be given. The complete correlation, as far as possible, of the pathologic and the clinical data for the entire series will be the subject of a separate communication.

CASE 32.—Fig. 12. Normal heart.

Clinical History.—A man, 63 years old, was operated on for an incarcerated inguinal hernia. Four months later, he developed signs of intestinal obstruction. Laparotomy and ileostomy were performed. He developed postoperative atelectasis, bronchopneumonia, and pulmonary embolism, and died thirteen days after the operation. He had never had any cardiac signs or symptoms.

Heart.—The heart weighed 420 gm. There were no valvular or other lesions, except a slight hypertrophy of the left ventricle, probably hypertensive in origin.

Coronary Arteries.—The coronary arteries showed only small scattered arteriosclerotic plaques, but no narrowings or occlusions, and no anastomoses. Their pattern with one exception was the same as that reported by Spalteholz in 80 per cent of human hearts. The exception was that the terminal branch of the left descending coronary artery turned back on the anterior surface of the heart. Ordinarily, when this branch extends beyond the apex, its termination is found on the posterior surface of the heart. The counterparts of the various anatomic landmarks labeled on this roentgenogram can be recognized easily on all the others. The various arterial branches are similar to those labeled in Fig. 11.

CASE 5.—Fig. 13. Angina pectoris, hypertension, arteriosclerotic heart disease.

Clinical History.—A woman, 60 years old, had suffered for two years before the first admission from dyspnea, palpitation, and substernal squeezing pain which radiated to the left shoulder. These symptoms occurred about once a month, and were relieved by rest. Examination revealed only an enlarged heart, and a blood pressure of 210/120. After total ablation of the thyroid the blood pressure dropped to 140/80, and the electrocardiogram showed normal rhythm, rate 95, low T_1, and inverted T_2 and T_3 of the coronary type. There were no anginal attacks and no dyspnea for nineteen months after the operation. After this, there were repeated anginal attacks which became increasingly severe and numerous. Death occurred thirty-four months after the thyroidectomy.

Heart.—The heart weighed 510 gm. There were no valvular lesions. The left ventricle was definitely hypertrophied. There were no infarcts. The myocardium showed no fibrosis grossly or microscopically.

Coronary Arteries.—The coronary arteries showed marked arteriosclerosis which was confined to relatively limited zones in the larger branches. From the roentgenogram alone it appears that the greater part of the left descending coronary artery is missing. The distal portion of this vessel with its wider lumen is well shown. Dissection revealed that in the apparently missing segment of this vessel there was so much arteriosclerosis (without calcification) that the vessel had been converted into a cord with a narrow, tortuous lumen. This lumen was discontinuous. On the roentgenogram is seen a brush of neighboring vessels which probably served as anastomotic channels. In none of them could a communication be traced between the proximal and distal end of the occluded artery. Many of these vessels are in the interventricular septum, for in this injected heart the septum was not removed before the roentgenogram was made.

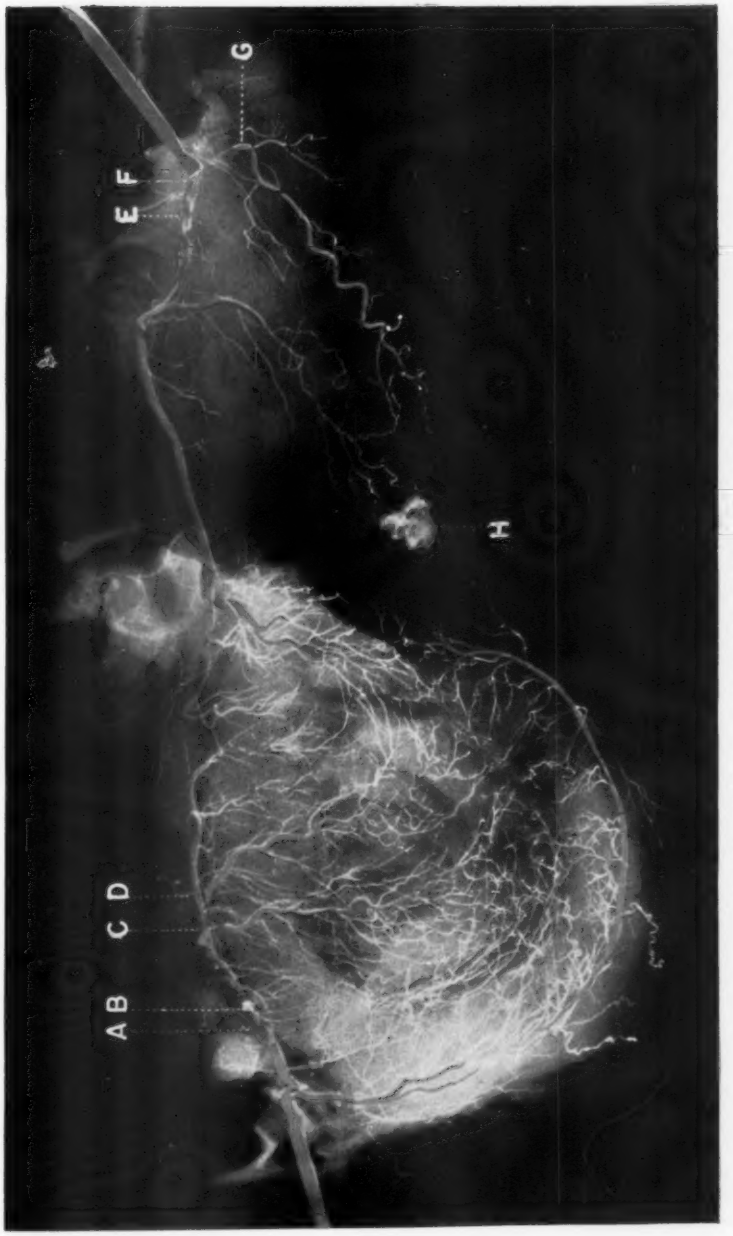

Fig. 13.—Case 5. (Illustration reduced to ⅗ normal size.)

A, Fresh thrombus
B, Calcified plaque
C, *D*, Narrowed branches (arteriosclerosis)
E, Narrowed lumen; calcified wall
F, Occluded lumen
G, Anastomotic injection
H, Artifact.

In the left circumflex coronary artery a different mechanism for occlusion is illustrated. There is much less arteriosclerosis in this vessel. The marked narrowing of the mouths of two of its main branches is well shown at *C* and *D*. Also, a calcified plaque is shown at *B*. Proximal to this plaque is found a zone, *A*, of complete occlusion by a freshly deposited thrombus. However, distal to this completely occluded zone, the remainder of this vessel was well injected with blue mass from the left coronary artery. Thus the whole left coronary system was well injected in spite of occlusion of its two main stems near their origins.

The whole right coronary system was likewise injected from the left coronary artery. No red mass in the right cannula flowed into any of the vessels. The main stem of the right coronary artery was completely occluded just at its origin, *F*. For a considerable distance distal to this point of complete occlusion there was marked narrowing of the lumen with calcification in the walls. This lumen shown at *E* was dissected open and found filled with the blue mass from the left cannula.

A point of special interest is the branch of the right coronary artery, marked *G*. It arose very close to the origin of this artery, and the right cannula was accidentally inserted distal to its origin. This vessel, nevertheless, was well filled with blue mass through an anastomosis from the left side. The shadow of an uninjected proximal portion extending almost up to the cannula can also be made out. Presumably, in the living heart, this vessel was the only branch capable of receiving blood through the right coronary orifice. If it had not been tied off before the injection, an altogether different pattern of anastomoses might have been found.

The irregularly shaped radiopaque area at *H* represents what would have been a hematoma in life. This heart was rather roughly handled during the injection procedure and the pericardium at this area was bruised. A few small branches must have been ruptured, for the mass leaked into the subepicardial tissues.

Comment.—The anastomotic circulation in this heart was so rich that it permitted an adequate injection throughout the heart in spite of the fact that both main branches of the left coronary artery and the main stem and a main branch of the right coronary artery were occluded at the time of injection. This anastomotic circulation was developing during the five years when the patient was having angina. Possibly the thyroidectomy prolonged the patient's life and thus afforded time for the rich anastomotic circulation to develop. This anastomotic circulation was so efficient that there was practically no fibrosis of the myocardium. Unquestionably, the final fatal insult to the heart was the deposition of the thrombus in the left circumflex artery, but because adequate anastomoses had developed in advance, no infarct resulted, and the patient died of cardiac failure.

A similar sudden occlusion without infarction probably could have occurred in the branch of the right coronary artery which was tied off from the cannula, since this vessel was likewise well injected from the left coronary artery. Judging from its wide-open connection with the right coronary artery, it can be assumed that the flow into this vessel in the living heart was largely from the right coronary artery, for the pressure gradient, in the sense of Wiggers,[15] must have been higher in this direction.

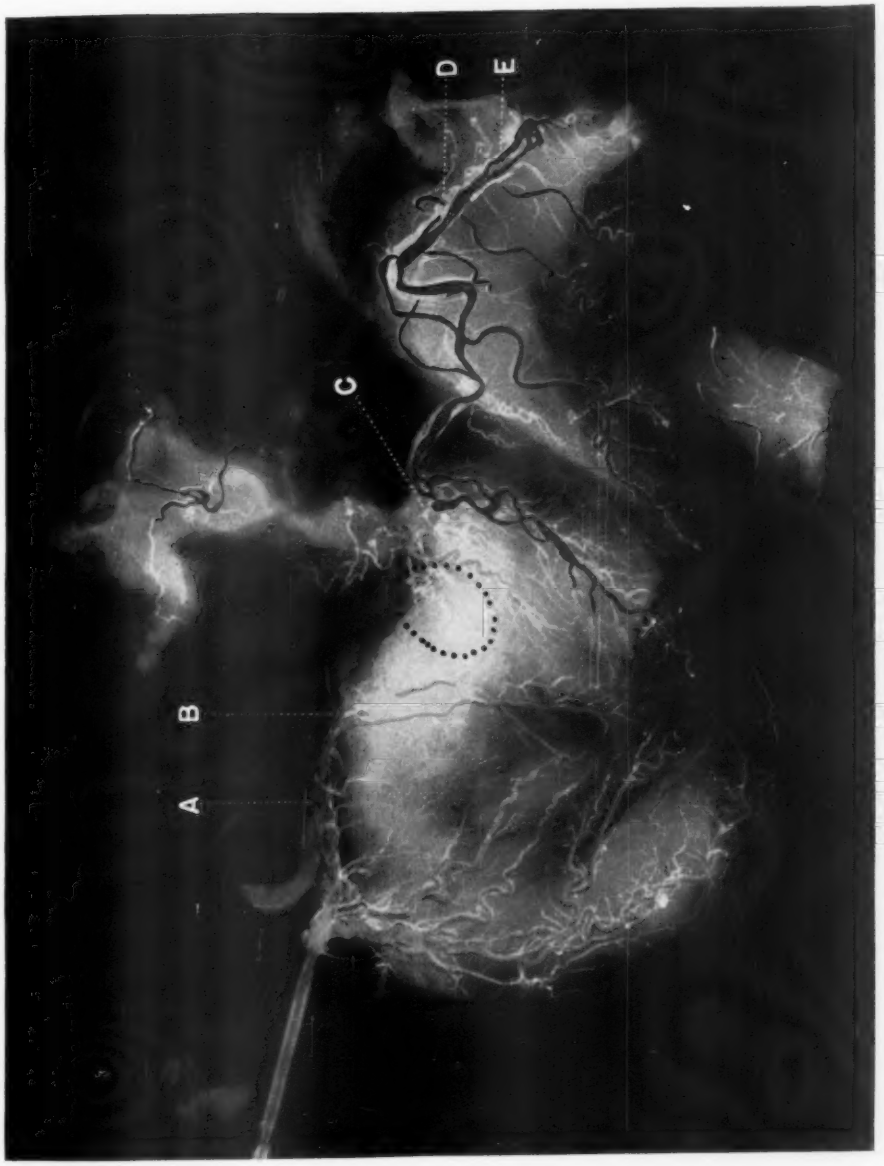

Fig. 14.—Case 18. (Illustration reduced to ⅗ normal size.)
A, *D*, *E*, Nonoccluding thrombi *B*, Occluding thrombus *C*, Old occlusion (arteriosclerosis).

CASE 18.—Fig. 14. Angina pectoris, mild hypertension, arteriosclerotic heart disease, mild congestive failure.

Clinical History.—The patient was a man, 69 years of age, who for two and a half years had had precordial pain brought on by exertion and accompanied by dyspnea and palpitation; he had lost a little weight, and complained of epigastric distress and anorexia. The first admission was one year ago for mild congestive failure. Examination at that time showed slight cyanosis, moderate enlargement of the heart, reduplication of the first sound at the apex, accentuation of the aortic second sound, and diminution in the intensity of the pulmonic second sound. The blood pressure was 180/110. The electrocardiogram showed normal rhythm, a rate of 80, left axis deviation, wide and notched QRS waves in all leads with intraventricular block, low T-waves in all leads. Another electrocardiogram two weeks later showed sino-auricular bradycardia, a rate of 48, and a diphasic T-wave. After digitalization and venesection, the patient was advised to take 0.1 gm. of digitalis daily, and was discharged. He was reasonably well for a year except for occasional attacks of precordial pain. These became more severe and more frequent about one month before admission, and were only partially, or not at all, relieved by nitroglycerin. The second admission was on account of a sudden large hematemesis which was probably due to the chronic gastric ulcer found at autopsy. In spite of transfusions and other treatment, he died on the fourth day.

Heart.—The heart weighed 380 gm. There were no valvular lesions. Microscopically the myocardium showed diffuse fibrosis. There was a small, old, healed infarct in the posterior wall of the left ventricle near the auriculoventricular groove. Its outline is indicated on Fig. 14 by the dotted line. There were no fresh or recent infarcts.

Coronary Arteries.—The coronary arteries showed marked arteriosclerosis with calcification and narrowing, but in most cases without occlusion. In the roentgenogram this arteriosclerosis is betrayed by the marked irregularity of the contour of all the large vessels. Several fresh stringy ante-mortem thrombi were present in these narrowed vessels. These had obviously been deposited just before death. In the roentgenogram their locations in the left circumflex and right coronary arteries are indicated by the letters *A*, *B*, *D*, and *E*. Neither thrombus in the right coronary artery, *D* and *E*, was large enough to cause complete obstruction. This was likewise true of the thrombus located at *A* in the left circumflex artery. However, the second thrombus, located farther along in this vessel, at *B*, had caused complete occlusion, and the vessel distal to this fresh occlusion was not injected. The shadow of the noninjected vessel beyond this occluding thrombus is plainly outlined, however, by the faint line of calcification in its walls.

A point of special interest is the terminal branch of the right coronary artery. In the roentgenogram this appears to be well injected, and not especially unusual. When dissected out, it was found to be entirely injected with blue mass from the left coronary artery instead of with red mass from the right coronary artery. The dissection disclosed a sharp, definite point of complete occlusion separating this terminal branch from the right coronary artery. This zone of complete occlusion was only about two millimeters long and is indicated at *C* in the roentgenogram. The anastomoses connecting this terminal branch of the right coronary artery with the left coronary artery were not traceable by dissection. Nevertheless, the roentgenogram shows several vessels which appear to bridge this gap.

Comment.—The roentgenogram of this heart well illustrates the varying pictures obtained in an extreme degree of widespread, marked coronary arteriosclerosis with calcification. Although this arteriosclerosis had gone on slowly to complete occlusion in the right coronary artery,

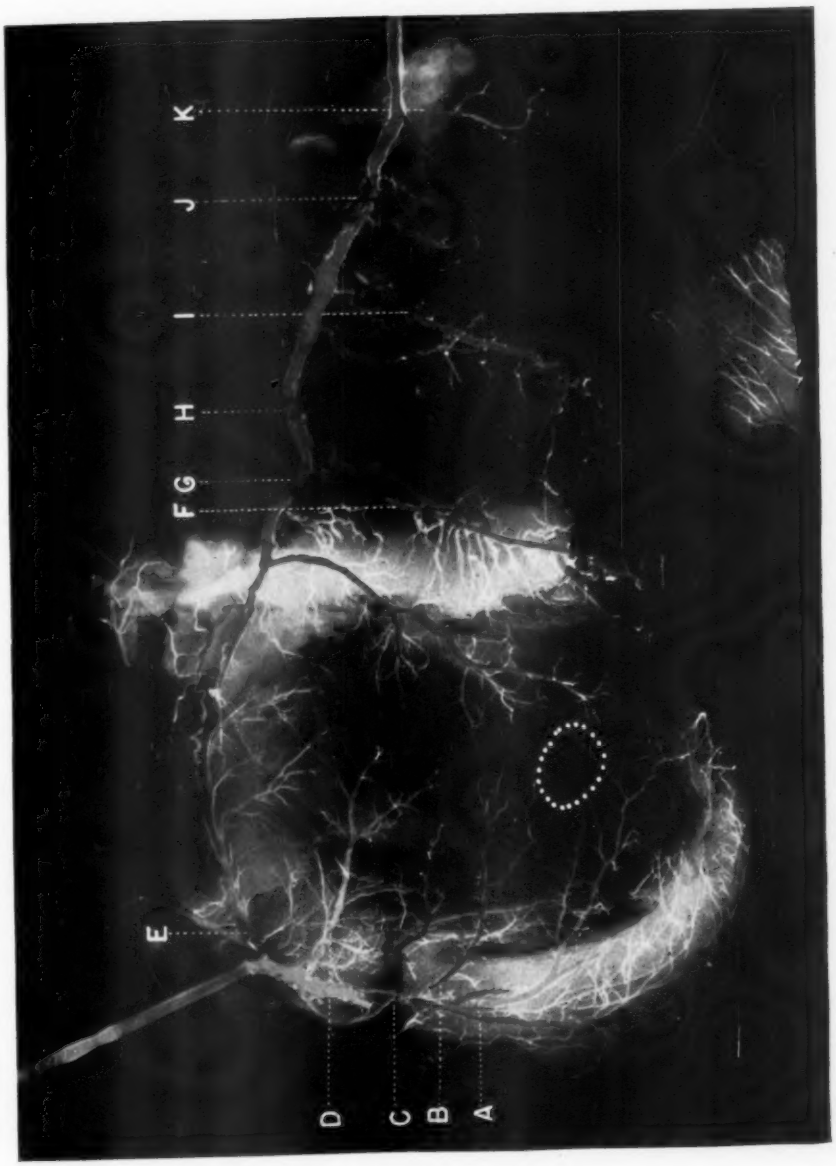

Fig. 15.—Case 11. (Illustration reduced to ⅔ normal size.)
A, B, C, E, F, I, K, Old arteriosclerotic occlusions with anastomotic injections
G, H, Embolic occlusions
J, Thrombotic occlusion.

such an efficient anastomotic circulation had been established that the small cardiac infarct which formed healed completely without presenting any signs or symptoms of acute coronary occlusion. However, there is little evidence for anastomoses elsewhere in this heart, for, when the termination of the left coronary was suddenly occluded by a thrombus, its distal portion remained uninjected.

CASE 11. Fig. 15. Severe angina pectoris, arteriosclerotic heart disease, multiple coronary artery occlusions with rich anastomoses, terminal thrombosis and coronary embolism.

Clinical History.—The patient was a man, 53 years old, who had had syphilis twenty years before and had recovered under treatment. For ten years he had suffered from pain in the precordium which was brought on by exertion and was relieved by rest. For three years the pain had been substernal and severe, radiating down the left arm, brought on by excitement or exertion, and relieved by nitroglycerin and rest. The attacks had been increasing in severity and frequency for two weeks. Twenty-two hours before death there occurred a more severe squeezing type of precordial and substernal pain, not relieved by nitroglycerin. Physical examination showed little except a gross irregularity of the heart and a pulse deficit. Three hours before death he had another attack of substernal pain and became cold and clammy. The blood pressure could not be measured, the pulse became imperceptible, and the heart sounds were very faint. It was thought that his heart had ruptured. He died three hours later.

Heart.—The heart weighed 350 gm. There were no valvular lesions and no rupture. The myocardium showed diffuse fibrosis throughout, and in the left ventricle there was one small area of marked thinning with almost complete replacement by fibrous tissue. This appeared to be a small, healed infarct. It is outlined by the dotted line in Fig. 15.

Coronary Arteries.—The coronary arteries showed marked arteriosclerosis which in numerous branches had gone on to complete occlusion and obliteration of the lumen for as much as 2 cm. at a stretch. Some of these are indicated in the roentgenogram at the points marked *A*, *B*, *C*, *D*, *E*, *F*, *I*, and *K*. In the left coronary artery such areas of complete occlusion (*C* and *E*) had broken the continuity of both the circumflex and the descending branches close to their origins. Nevertheless, both branches distal to the occluded zone were open and well injected, but the injection mass reached them by anastomotic channels from different sources. The left circumflex artery still received blood entirely from the left coronary artery as indicated by its content of pure blue mass. The left descending artery, however, was entirely filled from the right coronary artery with red mass. One of its branches, *A*, also entirely cut off from the main artery, was still receiving all its blood supply through an anastomosis with the stump of the left coronary artery. Another branch, *B*, less completely isolated, was receiving blood from both coronaries, as indicated by its content of purple mass.

The branch of the left descending coronary artery marked *D* deserves special consideration. In the roentgenogram, for a distance of 1 cm. from its origin it appears to be poorly injected and shows an irregular contour. Distal to this zone it appears to be well injected. When we attempted to open this vessel, no lumen was found up to a point just proximal to its bifurcation. The entire proximal part was a solid calcified cord. This calcified cord appears in the roentgenogram as if it were patent and completely injected with the radiopaque mass. This illustrates another of the pitfalls which are encountered when the coronary circulation is studied by any method, whether corrosion, clearing, or x-ray, which does not also include a thorough dissection of the vessels as part of its routine.

In the right coronary artery, the lumina of many of the major branches (*F*, *I*, and *K*) were separated from the lumen of the main stem. These branches are all well injected, however, one from the right coronary artery, one entirely from the left, and one from both coronary arteries. In the roentgenogram in some places (*F* and *I*) there appear to be quite large, newly formed, bridging, anastomotic channels. None of these could be dissected out to show actual continuity of the lumen.

In the main stem of the right coronary artery near its origin, at *J*, there was a large atheromatous ulcer with a freshly deposited, soft, ante-mortem thrombus adherent to it. This thrombus had caused practically complete occlusion at this point. At two points (*H* and *G*) farther along in this same vessel, there were loosely attached blood clots which completely occluded the lumen. These were found in portions of the vessel which were somewhat narrowed by atheromatous patches, but without any ulceration present. They were interpreted as emboli which had broken loose from point *J*.

Comment.—In this heart, in spite of multiple points of complete coronary artery occlusion, there was only one small, old, healed area of infarction. In the ten years during which the patient had had repeated anginal attacks, a new and very complicated anastomatic circulation had been set up. The numerous lesions of the coronary branches must have progressed so slowly to complete occlusion that sufficient time was afforded, in all instances, for the development of adequate anastomoses.

The special features of the terminal episodes are also reflected in the heart. The severe attack which brought the patient to the hospital was probably coincident with the deposition of the thrombus on the atheromatous ulcer near the origin of the right coronary artery. Although this had occurred twenty-two hours before death, there was no indication of the beginning of an infarct in the area supplied by this vessel, and no large area of the myocardium was avascular. Thus, in a heart with such a rich anastomotic circulation, the sudden occlusion of even a large vessel may not result in an infarct. Probably such sequences had occurred at numerous times during the preceding ten years. It is also probable that the patient would have survived this occlusion had not a second and a third severe insult to the heart occurred soon afterward. These also resulted from the thrombus described above. The sudden collapse three hours before death was probably synchronous with the passage of part of this thrombus, as an embolus, farther along the vessel. This sequence of events is supposed by many to be rather rare. Here also, if the blood clots interpreted as emboli had been found lying free in the vessel, rather than lightly adherent, there might have been some suspicion that the injection procedure had dislodged them from their original location.

Case 19.—Fig. 16. Coronary thrombosis, cardiac infarct, rupture of the heart.

Clinical History.—The patient was a man, 50 years of age, who had been admitted to the hospital three years before with paroxysmal tachycardia and breathlessness. The electrocardiogram then showed left axis deviation, a diphasic T_2 and inverted T_4. Under quinidine therapy, the heart rate quickly returned from 160 to normal. The patient said he had had several similar episodes during the previous

year. Three years later, for one week, he had daily substernal pain associated with marked dyspnea. These attacks were induced by mild exertion, exposure to cold, or excitement, and were relieved promptly by nitroglycerin. Finally, he had a more severe similar attack, lasting an hour, and accompanied by pain radiating down the left arm. On admission, the electrocardiogram showed normal rhythm, a rate of 90, left axis deviation, slight elevation of the S-T segment in Lead III, and a flat T_4. Five days later, the electrocardiogram showed a rate of 110 and elevation of the S-T segment in Leads III and IV of the acute coronary type. The temperature was normal on admission, but next day rose to 102° F. and remained elevated until death. The blood pressure remained between 110/80 and 130/90. He had repeated attacks of substernal pain, usually relieved by nitroglycerin or morphine. On the fourth day, he suddenly became ashen and very short of breath, and expired. Autopsy showed that the heart had ruptured, producing hemopericardium.

Heart.—The heart weighed 430 gm. There were no valvular lesions. There was a large, fresh infarct in the posterior wall of the left ventricle. The extent of this infarct is indicated in Fig. 16 by the dotted line. At the anterior border of this infarct there was a tear of the myocardium 1 cm. long, indicated by a broken line. Elsewhere the myocardium was not unusual.

Coronary Arteries.—The coronary arteries showed only slight diffuse, but considerable localized, arteriosclerosis. Not a single plaque was found in the right coronary artery. A single small plaque (*A*) was found in the left descending coronary artery. The condition of the left circumflex coronary artery is of prime interest. In this vessel, a short distance from its origin, was an extensive area of arteriosclerosis with considerable narrowing, without calcification. This is shown in the roentgenogram at *B*. Deposited on this latter plaque was a large, occluding, dumbbell-shaped thrombus. No injection mass went past this thrombus, for the intima of the vessel in this region was entirely untinted over a length of about 7.0 mm. In the roentgenogram there is complete absence of shadow of injection mass in this zone. Nevertheless, the lumen of the open vessel just distal to this occluded zone shows a faint shadow of injection mass. On dissection, the intima here was found to be tinted pale blue, thus indicating that this injection mass had come entirely from the left coronary artery. Branches originating in this portion of the vessel distal to the occlusion were similarly injected. It is evident from the roentgenogram that this injection was by anastomotic channels from branches of the left descending artery. Again, although it was not possible to be sure about the dissection of such branches, several links which seem to connect can be found in the roentgenogram.

Careful study of the roentgenogram reveals the outline (*D*) of the left circumflex artery and its branches distal to this zone of anastomotic injection. In this region, however, the shadow of the lumen is less radiopaque than the surrounding heart tissue, rather than the reverse, as is the case when the lumen is filled with the mass. This is due to the fact that the vessel was distended with the salt solution which was used as a preliminary wash. The salt solution evidently ran into this vessel through the anastomotic channels more readily than did the injection mass. Probably if the injection pressure had been raised above the usual standard (150 mm. Hg), or if the injection time at this pressure had been prolonged, the injection of this vessel would have been more complete.

Comment.—In this heart the slow narrowing of a single coronary artery branch, followed by rapid occlusion of that branch and then sudden death four days later from rupture of the heart, presents a sequence of events such as one might plan experimentally. We have repeatedly found that in the normal heart the ligation of a single vessel just previous to injec-

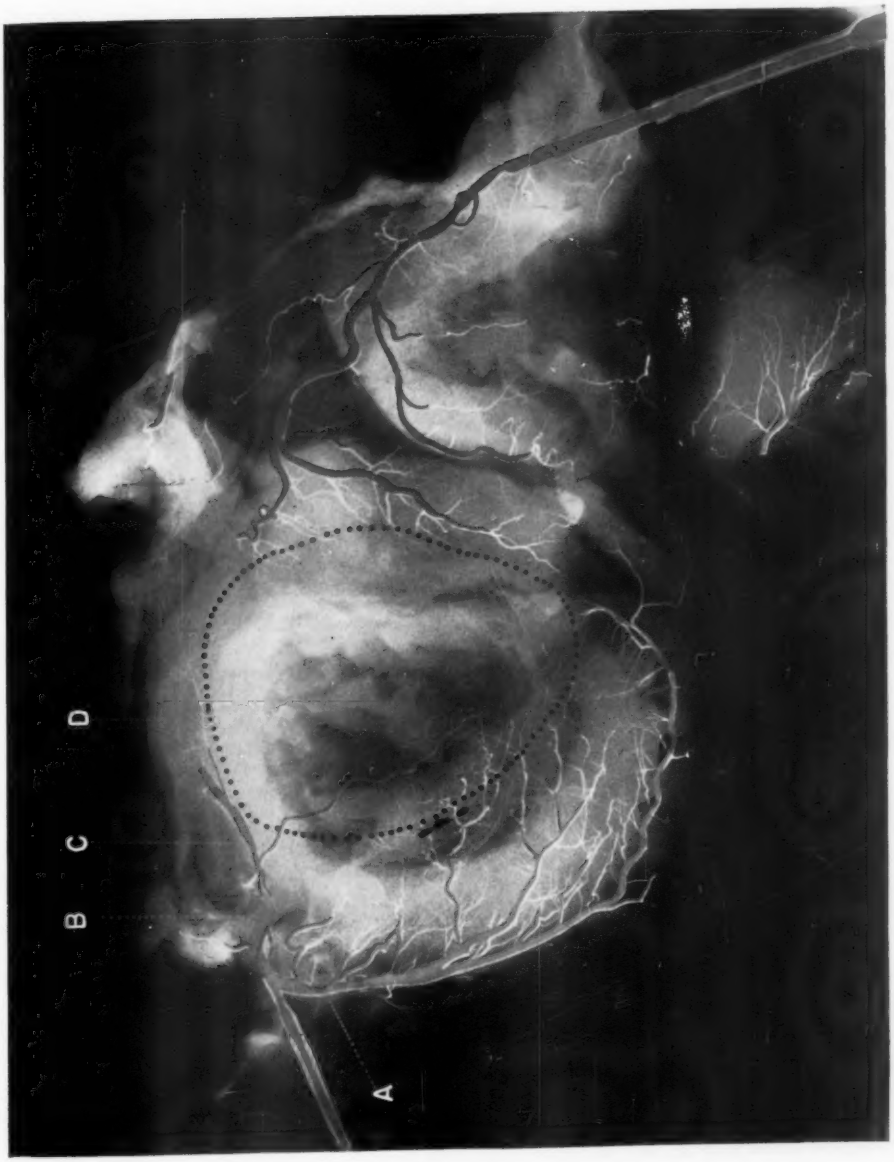

Fig. 16.—Case 19. (Illustration reduced to ⅔ normal size.)
A, Arteriosclerotic plaque
B, Occluding thrombus
C, Anastomotic injection
D, Uninjected vessel.

tion never results in anastomotic injection beyond the ligature. The anastomoses found in this heart bridging the completely occluded zone probably did not develop during the four days between the sudden acute occlusion and death. It seems more probable that they were being established during the progressive course of the gradual narrowing of the left circumflex artery. The slow narrowing could probably have gone on to complete occlusion without the formation of an infarct. The sudden thrombotic occlusion before the anastomotic circulation was ready resulted in infarction and death.

DISCUSSION

There are two essentially new procedures in the method here described for studying the cardiac circulation: First, a dissection of the heart was devised which unrolls the unfixed heart in such a way that the complete coronary artery tree is laid out in practically one plane, resembling a diagram. Second, a new radiopaque injection mass which permits such a dissection of the fresh, unfixed heart was used. The basis of this mass is a solution of agar-agar. To this an insoluble lead salt was added. Although it is ideal for this purpose, agar has been seldom so used. It can be kept indefinitely in liquid form at a comparatively low temperature (45° C.), can be immediately hardened by chilling, and will not liquefy again at room temperature. None of the various metals, waxes, starches, gums, celloidin, or gelatin previously used are as satisfactory as agar. Lead was arbitrarily selected for the radiopaque substance because of its high molecular weight and high relative radiopacity in comparatively low concentrations. However, since there are no limitations due to the dangers of toxicity as there are in the living patient, other metals, such as bismuth or mercury, might prove to be more satisfactory than the more commonly used barium. Complications such as the effect on the solubility and coagulability of the agar, uniformity and small size of the particles, effect on the tissue injected, etc., enter into such a selection. We have used the lead phosphate agar as prepared above throughout this series because it was the first to prove satisfactory, but we are continuing our experiments with various other methods of preparation and various other salts in combination with the agar base.

Direct comparison of this lead-agar with the more commonly used barium-gelatin has shown that we obtain as satisfactory roentgenographic shadows with 15 per cent lead phosphate as with 30 per cent barium sulfate. The gelatin, of course, remains solid at room temperature only after fixation in formalin. At the injection temperature of 45° C. the lead-agar is considerably more fluid than the barium-gelatin. Relative to human heparinized blood at 37° C., and tested on the same viscosimeter, the lead-agar has a viscosity of three and the barium-gelatin of eighteen. This extremely high viscosity of the barium-gelatin is due to

its high content of both gelatin and barium sulfate. It is desirable to keep the viscosity of the injection mass as low as is consistent with the other properties which such a mass must have. The great difference in the viscosity of these two masses is, however, not directly reflected in their ability to penetrate into the small arterioles. Both reach vessels of about the same caliber. For arterial visualization, an injection mass which would pass through the capillaries would be useless, but it should penetrate almost to them. The size of the largest particles present in the mass is probably an important factor in this uniform penetrability. Our ultimate aim is to prepare a mass which will have the desirable properties of the present lead-agar mass, but will give an even more detailed picture of the coronary artery tree.

In the procedure as described, it is easily possible, with the dissecting scissors, to open up and follow vessels of a diameter of 1.0 mm., or slightly less, especially when their intimas are brightly colored and the vessels are filled with a mushy agar plug. We regularly lay open all the coronary arteries as far as branches of that caliber in all injected hearts. If the vessels are not opened, they may be traced even further as thin, white, pencil lines, due to their content of semisolid injection mass. Only on rare occasions, however, have we been able to connect two open lumina by white streaks which could not be opened. By actual micrometer measurements on the roentgenograms, we know that vessels with lumina as small as 200 micra are regularly visualized. The finest twigs shown in the roentgenogram can never be dissected out, of course. Measurements with the micrometer ocular on the microscopic sections show that in normal hearts the lead-agar mass always penetrates to arterioles 40 micra in diameter, reaches about 50 per cent of the vessels 20 micra in diameter, and never injects vessels smaller than 10 micra in diameter. Table V sums up these various measurements and the conclusions to be drawn from them. The general statement can be made that, with the method used, anastomoses, when they occur, are present in small arterioles only.

TABLE V

ZONES OF CORONARY ANASTOMOSES

ZONE	DIAMETER OF VESSEL (MICRA)	METHOD OF PROVING CONTENTS OF VESSEL	ANASTOMOSES
1	> 800	Lumen opened with dissecting scissors	Anastomoses proved only once
2	800 to 501	Dissectible but without opening lumen	Anastomoses rarely proved
3	500 to 201	Visualized by x-ray but not dissectible	Anastomoses probable but unproved
4	200 to 40 to 10	Injected but not visualized by x-ray	Anastomoses usual and proved
5	< 40 to 10	Not injected by mass	Anastomoses ?

There is a large, unexplored territory between arterioles of these dimensions and the capillaries. In this territory lie the vessels to the

valves which we have never succeeded in injecting with the lead-agar. The connections with the Thebesian channels will also be found in this uninjected territory since there was never any leak of the injection mass into the chambers of the heart. Information on these problems awaits the preparation of a more nearly perfect mass. Injections of these structures in continuity with the coarser circulation will yield many new facts. The method of unrolling the heart and laying out all these structures in one plane should permit many new studies to be made. The data presented above apply only to the arteries of the ventricles. The auricular branches are less constant in their origin and course and practically never become occluded. The few branches going to the auricles are easily followed in the roentgenogram of the unrolled heart. Their paths will be the subject of a separate communication.

The dissection devised for the purpose of disentangling the arteries has unexpectedly proved to be superior in other respects to the traditional incisions for opening the heart. After this dissection all the endocardial structures are simultaneously available for inspection on one side of the specimen, and all the pericardial surface on the other side. It is much the same as opening a single-chambered hollow viscus, such as the stomach. When it is desired to open the heart only for a routine examination, the complete dissection is slightly modified. A single incision through the middle of the interventricular septum from the base of the heart to the apex is then substituted for the incisions devised to remove this septum.

Except for the reading of the roentgenograms and the final detailed dissection of the doubtful vessels, the method described is simple enough so that it can be entrusted entirely to a technician. The conditions of the injection are definitely standardized and constant, and require almost no adjustment in individual hearts. In our more recent series unsuccessful injections are rare, even in the hands of an assistant unskilled in the use of the method. A surprising amount of information about the condition of the circulation in an individual heart, much of which would otherwise have been overlooked entirely, can be obtained from even a partially successful injection by this method. We have never had an uninstructive roentgenogram.

We have placed so much emphasis upon the method used because it is our belief that much of the confusion in the literature about the effect or lack of effect of occlusions of the coronary arteries and the ability of the collateral anastomotic circulation to compensate for such occlusions is due to unsatisfactory methods of study. No absolute statements on the above questions could be made for any individual heart unless *every* artery down to the smallest arteriole had been examined. The nearer the method approaches that ideal, the better the results. For each individual vessel, one must know whether it is patent throughout its whole

length, and, if patent, what is the source of its blood supply. Only if all these data were available, could one fully interpret the possible effects of such occlusions as may be found.

The combination of a multicolored radiopaque injection material and a complete dissection gives more information than any other method yet devised. Injections without dissections, no matter whether visualized by corrosion, clearing, or x-ray, miss occlusions and appear to show anastomoses between large vessels which actually do not exist. Dissections without injections miss occlusions also and are notoriously incomplete in other respects. Repeated reference to the roentgenogram of the injected vessels in the unrolled heart during the course of the dissection serves as a constant stimulus to attempts to dissect out anastomotic channels apparently present in the roentgenogram. Also, the distribution of the multicolored injection mass in the arteries as they are opened directs attention to possible and unsuspected channels of flow shown in the roentgenogram. At the end of such a dissection one is justified in concluding that every possible occluded spot in the coronary artery tree has been found and that an attempt has been made to dissect out every possible anastomotic channel. Conversely, when no occlusions or anastomoses can be found, one is equally sure that none existed. Our confidence in these conclusions has been built up only after many exasperatingly unsuccessful attempts to dissect out an anastomotic connection which we knew must be present. When the whole right coronary system has been injected with the blue mass from the left coronary artery, as in Fig. 13, or when the vessels throughout show a variegated picture of red, blue, and various shades of purple in the vessels supplied by both cannulae (Fig. 15), there must be a very rich anastomotic circulation present even if it cannot be followed with the dissecting scissors or in the roentgenogram.

Thus, for final proof of anastomosis, we rely very little on the roentgenogram or on our ability to dissect out the actual connecting channel. These procedures give evidence of the amount and distribution of arteriosclerosis and points of narrowing and of occlusion. The evidence for anastomotic circulation is drawn largely from the distribution of the multicolored mass in the dissected vessels. In this group of 35 hearts taken from patients over 50 years of age, these procedures taken altogether have shown a rich anastomotic circulation in only those hearts in which there was occlusion of the coronary arteries. Such zones of anastomotic circulation were not distributed indiscriminately, but in each individual heart the anastomoses were specifically designed to compensate for the occlusion. The compensatory blood supply usually came from the left coronary artery, no matter where the occlusion was, but the reverse was occasionally true. However, with this method which so readily showed the intimate details of an anastomotic circulation when

it was present, we could not demonstrate any anastomoses in normal hearts in which there were no occluded coronary arteries. Others who have reported coronary artery anastomoses in normal senile hearts usually give few data as to their criteria for the selection of "normal" hearts. Throughout their reports, increase in the amount of arteriosclerosis with increase in age is tacitly acknowledged. The amount of arteriosclerosis which they accept as "normal" for each age group is not clear. Our series is at present too small to permit grading of the amount of arteriosclerosis in each age group. Inasmuch as there is a direct relation between the degree of anastomosis and the degree of arteriosclerosis in the series as a whole, we feel that a similar relation will be found within each age group. It thus seems that anastomoses in the coronary artery system do not develop *pari passu* with increase in age, but only when and where there is need for them. Then and there they develop quite easily and readily and usually to a sufficient degree to compensate adequately.

From an anatomical viewpoint this may appear to be a satisfactory circulation. It seems, however, that there must often be a greatly disturbed physiologic balance. Thus when, as in Fig. 13, the blood flow through the whole of the right coronary artery moved from its narrower peripheral end to its wider, more central end, there must have been some functional disarrangement of the flow. The arteries do not serve as mere inert tubes for the passage of blood, but their complicated muscular and elastic tissue walls are also concerned in the local control of that flow. When the flow through a vessel is in the opposite direction to that for which the artery was designed, there must be some disturbance of function. Such disturbances must occur on occasion in different locations in hearts in which certain parts are being nourished by an anastomotic circulation. Perhaps this flow in the wrong direction, so to speak, has some relation to anginal pains.

The emphasis throughout this report has been upon coronary artery occlusions and anastomoses. We have studied five hearts without occlusions, but with anastomoses. They were from patients whose ages varied from 5 to 77 years. None showed more than a few scattered plaques of coronary arteriosclerosis. All these hearts, however, were markedly abnormal in other respects. Other equally abnormal hearts (but without arteriosclerosis or occlusions) showed no anastomoses. Thus, although coronary artery occlusion is the commonest cause of the development of coronary artery anastomosis, it is not the only one. Only a complete study of a larger series of hearts which are the seat of pure valvular disease or have been damaged by hypertension will explain why some develop anastomoses and other do not. Probably here also these anastomoses develop only when and where they are needed.

When an artery is completely occluded, the need for a new channel to carry the blood around the obstruction is obvious. Arteriosclerosis, the outstanding cause of occlusions, is a slowly, steadily progressing lesion, with much narrowing before the final complete block. This narrowing, in itself, surely creates a need for anastomoses, and, as illustrated in Case 19, the anastomoses form. With the proper technique, it is comparatively easy to find all complete occlusions. It is much more difficult to make even a rough estimate as to how much partial obstruction is present at any one spot. Although Saphir and his associates concluded that at least two vessels must be affected to give rise to an infarct, in their series of 30 infarcted hearts only 11 (37 per cent) showed complete occlusion in branches of two of the three major divisions of the coronary arteries. Four (66 per cent) of the six more carefully studied infarcted hearts we examined showed such double occlusions. Many of the hearts we studied showed marked arteriosclerosis in two or more major branches without infarcts. The important point to emphasize is not the multiplicity of the lesions in the coronary arteries, but the speed with which the occlusion or narrowing develops. A rapid occlusion in one major branch, with all other branches normal, will result in an infarct, as in our Case 19. Slower narrowings, even if numerous, stimulate the development of anastomoses, and the heart is thus prepared for occlusion when it comes.

The roentgenograms of the unrolled injected vessels help greatly in the study of the relative vascularity of the right and left ventricle at various ages and under varying pathologic conditions. The length, caliber, and method of branching of every vessel can be plainly seen. We are at present measuring these factors in order to correlate them with the weight, thickness, and nature of the disease of the myocardium of the two ventricles. The obvious excess of the number of branches of the left coronary artery over the right is the only clue we have at the present time as to why occluded branches in either artery usually obtain at least some of their compensatory channels from a branch of the left coronary artery.

Even in normal hearts there is a consistent absence of large vessels over a small area in the posterior wall of the right ventricle near its base. This apparently avascular area is very thin and never fibrosed. Infarcts in this area are very rare (Saphir did not find one), and it seems probable that normally it is largely nourished by the Thebesian vessels. Investigators of these vessels might well concentrate on this area.

CONCLUSIONS

1. The coronary arteries, in *normal* human hearts, even senile hearts, are true Cohnheim end arteries, without anastomotic connections; such anastomoses do not develop *pari passu* with increase in age.

2. Anastomoses always develop readily *whenever* and *wherever* arteriosclerotic narrowing or occlusion causes obstruction in the coronary artery circulation; these anastomoses are localized to the regions where they are needed.

3. To ascertain accurately the site and effects of all coronary artery occlusions and anastomoses in individual hearts, it was necessary to devise a method capable of *completely* and *simultaneously* visualizing the *entire course* of all arterial branches so that they could be studied in detail. This has been accomplished by a simple standardized method utilizing (a) a newly devised multicolored radiopaque injection mass, (b) a new method of cutting open the injected heart, and (c) a complete dissection of the colored coronary artery tree.

4. The new injection mass consists of a suspension of lead phosphate in agar, colored differently for the right and left coronaries. It is injected at 150 mm. Hg pressure, at 45° C.; it sets quickly and permits immediate cutting and radiography of the fresh unfixed heart.

5. The new method of opening the heart unrolls all the coronary arteries so that they lie in one plane and avoids overlapping of the roentgenographic shadows of the injection mass within them.

6. The distribution of the multicolored mass in the dissected coronary artery branches gives an absolute index of the distribution of the blood from either coronary artery orifice.

In the preparation of the roentgenograms, the helpful cooperation of Dr. Samuel A. Robins, and the technical skill and always willing assistance of Mr. Nathan L. Shapiro, both of the X-ray Department of the Beth Israel Hospital, are gratefully acknowledged.

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THE ROLE OF NUTRITIONAL DEFICIENCIES IN THE PRODUCTION OF CARDIOVASCULAR DISTURBANCES IN THE ALCOHOL ADDICT*

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IT IS well-known that alcohol addicts who have no history of cardiovascular or kidney disease, and no demonstrable arteriosclerosis or persistent hypertension, frequently show signs and symptoms referable to disturbances of the circulatory system when they have recovered from the immediate effects of their inebriety. This study was undertaken in an effort to clarify the nature and relative frequency of these manifestations, and to evaluate the relative importance of alcohol and dietary deficiency as etiologic factors. The latter is of especial significance because other complications of alcohol addiction, such as polyneuritis,[1-5] pellagra,[6, 7] and alcoholic stomatitis[8] have been shown to be due to dietary deficiency rather than to the direct action of alcohol.

SELECTION OF CASES

The 83 subjects of this study were the alcohol addicts between the ages of 27 and 51 years, inclusive, who were admitted to this service during the year ending June 1, 1937, for treatment of the conditions indicated in Table I, who did not have and never had had, as far as we could ascertain, chronic cardiovascular or acute or chronic kidney disease, and had improved or recovered when they were discharged from the hospital.

Eighteen of these 83 patients showed none of the stigmas (Table I) of alcohol addiction. The diagnosis of alcohol addiction was made in

TABLE I

DISTRIBUTION OF COMPLICATIONS IN THE ALCOHOL ADDICTS STUDIED

	WITH PERIPHERAL NEURITIS	WITHOUT PERIPHERAL NEURITIS	TOTAL
Peripheral neuritis only	25	–	25
Alcoholic encephalopathy or Korsakoff's syndrome	16	2	18
Pellagra*	12	0	12
Laënnec's cirrhosis	7	2	9
Scurvy	1	0	1
Total complicated	61	4	65
Uncomplicated			18
Total subjects			83

*Includes two cases of alcoholic stomatitis.

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this group of "uncomplicated" subjects on a record of at least two admissions to the alcoholic ward of this hospital within one year previous to the time when they were selected for study.

METHODS

Upon admission to the medical service each patient was given the basal diet[4] which is of borderline adequacy in its content of vitamin B_1 for persons weighing from 58 to 63 kg.; the intake of fluid and salt was not restricted. Only those who, because of the severity of their peripheral neuritis or encephalopathic manifestations, were unable to be up and about the wards were kept in bed. During this preliminary period, which lasted from four to fourteen days, no specific medication was given, and the cardiovascular status of each subject was studied. This study included (1) a history of the present illness, covering the diet and any previous acute or chronic diseases, as elicited from the patient and verified, whenever possible, through friends and relatives; (2) detailed physical examination at daily intervals, including daily weighing; (3) complete blood count; (4) plasma protein determinations within twenty-four hours following admission to the medical service; (5) repeated blood pressure determinations; (6) a teleoroentgenogram of the heart; (7) an electrocardiogram using the three standard leads, made as soon as the subject was able to cooperate; and (8) complete urinalysis, which was repeated if indicated.

At the completion of the above studies, and after the patient had reached a constant weight level, the 65 patients with complications who showed in addition to their alcohol addiction one or more of the diseases listed in Table I were maintained with a weighed diet rich in vitamins, supplemented by 18 gm. of vegex daily. In addition to 3,100 calories, this regimen supplied 1,065 international units of vitamin B_1 daily, which was approximately four times their estimated maintenance requirement of vitamin B_1.[9] This therapy was maintained for periods varying from two weeks to two months. In ten instances the oral therapy was supplemented by daily intravenous injections of 10 mg. of crystalline vitamin B_1,[10] and three patients received 50 mg. of crystalline vitamin B_1 daily by parenteral administration. The studies outlined above were repeated at intervals throughout the period of observation and again before discharge.

The 18 alcohol addicts who showed none of the stigmas of alcohol addiction did not receive specific treatment, and the initial studies were not, as a rule, repeated.

RESULTS

The data accumulated were analyzed by two methods. First, a comparison was made in the group with complications before and after the period of vitamin therapy. Second, observations made during the control period on the group with complications were compared with those made on the group without complications.

The results by the first method of study are summarized in Table II and are described below. Eight (12.3 per cent) of the entire group of 65 patients complained of cardiac palpitation on admission to the medical wards. Twelve (18.4 per cent) were troubled by shortness of breath on slight exertion. Two complained of pain over the heart in addition to shortness of breath, and one complained only of precordial pain. Three patients presented marked cyanosis of the nail beds on admission to this service. These signs and symptoms were present singly or in combination in a total of 19 of the subjects (29 per cent). In

every instance these evidences of cardiovascular dysfunction disappeared within four days following admission to the medical wards, and before any therapy other than sedation was instituted.

Mild to severe edema was present in 20 patients, two of whom had anasarca. In addition to the edema, 18 of these patients (90 per cent) showed other signs of circulatory distress. On admission, 13 had one or more of the following symptoms: palpitation, dyspnea, precordial pain, cyanosis. In 12 instances the liver was enlarged and palpable, and 4 of the patients had cardiac murmurs.

TABLE II

INCIDENCE AND TYPE OF CARDIOVASCULAR DISTURBANCES IN THE GROUP WITH COMPLICATIONS AND INCIDENCE OF CHANGES FOLLOWING THERAPY

	NO. OF CASES ON INITIAL STUDY	NO. OF CASES IN COL. 1 IN WHICH STUDIES WERE REPEATED AFTER THERAPY	NUMBER IMPROVED AFTER THERAPY	PER CENT IMPROVED
Symptoms due to cardiovascular dysfunction	19	19	19	100.0
Edema	20	20	20	100.0
Palpable liver	26	26	14	53.9
Cardiac murmurs	9	9	8	88.9
Enlarged heart (x-ray)	14	8	4	50.0
Systolic blood pressure above 150	15	15	14	93.3
Diastolic blood pressure above 100	9	9	8	88.9
Abnormally large value for $K : Q\text{-}T = K \sqrt{R - R}$	20	10	5	50.0
Low voltage of QRS in all 3 leads	1	1	1	100.0
Low voltage of T-waves in all 3 leads	6	4	3	75.0
Inverted T-waves in 1 or more leads	25	15	11	73.3
Depressed S-T segments	10	10	10	100.0
Right axis deviation	3	3	3	100.0
Left axis deviation	16	7	4	57.1

In 12 cases the edema disappeared after the first day in the hospital and did not recur, although these patients were kept out of bed as much as possible during the day. Three patients on our basal diet,[4] with an unrestricted fluid intake, and without absolute bed rest lost their edema gradually over a period of three or four days. In 4 cases the edema did not disappear until after the institution of high vitamin therapy. In one patient who showed anasarca on admission, mild pitting edema of the lower extremities was still present when he was discharged fifty-one days later.

Sixteen patients who presented the above signs and symptoms of cardiovascular dysfunction had enlarged, palpable livers on admission. In 12 instances the enlarged liver was associated with edema, and in 7 of these the liver had decreased greatly in size or was no longer palpable at the time of discharge from the hospital. A definite diagnosis of hepatic cirrhosis was made in 3 instances in which the liver remained unaltered in size. The liver decreased considerably in size in one patient in whom a diagnosis of cirrhosis had been made.

Enlarged livers were palpated on admission in 10 patients who presented no other clinical evidences of cardiovascular disturbance. In 7 instances the liver was no longer palpable at the completion of the study period. One patient with cirrhosis revealed no alteration in the size of the liver, and another with a diagnosis of cirrhosis showed, after institution of the high vitamin regimen, a decrease in the size of the liver to a point where it was no longer palpable when he was discharged.

The average heart rate at the completion of the period of hospital care was 92, as compared with an average of 101 on admission.

Of the 9 patients with cardiac murmurs on admission, 3 had systolic murmurs heard only at the apex. In 2 cases a systolic murmur was audible only over the aortic area; a systolic murmur audible at both base and apex was heard in 3 instances; systolic and diastolic murmurs at the base alone were present in one case. Persistence of a murmur throughout the period of hospitalization occurred in only one instance; this patient had a short rough systolic murmur over the aortic area which was not transmitted.

Of the 14 patients with roentgenographic evidence of cardiac enlargement, 7 had left axis deviation; one had right axis deviation; and 6 had no abnormal deviation of the electrical axis. Teleoroentgenograms were repeated before discharge in 8 instances, in 4 of which the size and the shape of the heart shadow were within normal limits. Of these 4 patients, one had shown right axis deviation, and 3 left axis deviation; all returned to normal before the final teleoroentgenogram. In only one of the four subjects whose cardiac enlargement persisted was there an associated deviation of the electrical axis (left) throughout the period of observation.

A comparison of the average admission blood pressure of the group without complications with that of the group with complications does not reveal significant differences. These figures, however, require further analysis. If the patients admitted in circulatory collapse are omitted from the group with complications, we obtain a value of 141/90, as compared with 134/84 for the group without complications. We find also that in the complicated cases there was a range in blood pressure values from 106/70 to 190/120, with systolic blood pressures above 150 in 15 cases (23 per cent) and with diastolic blood pressures of more than 100 in 9 (13.8 per cent). The range in blood pressure values in

the group without complications was 110/70 to 160/100 with only 2 patients (13 per cent) presenting a systolic pressure over 150, and none a diastolic pressure above 100.

Analysis of the final blood pressure readings in the complicated cases reveals a range of 95/60 to 162/105, with an average of 121/81. At the time of discharge only one patient (1.5 per cent) presented a systolic pressure above 150, and only one (1.5 per cent) a diastolic pressure above 100.

In 20 subjects (30.7 per cent) the relation of ventricular systole (Q-T interval) to the entire cardiac cycle (R-R interval), as measured in the initial electrocardiograms and expressed by the constant K of Cheer and Dieuaide,[11] was above the normal values (0.433 for males and 0.456 for females) of Shipley and Halloran, as given by Feil.[12] Tracings were repeated before discharge in 10 instances. In 5 the value of K returned to normal limits. In no case was there an increase in K above that calculated from the initial electrocardiogram. In 4 of the 45 patients (69.3 per cent) whose initial values for K were within normal limits a later rise above normal occurred. We were unable to correlate the changing values for K with variations in the heart rates of these patients. Seventeen (85 per cent) of the group of 20 patients with high initial values for K showed clinical evidence of cardiovascular dysfunction on admission, but 14 (31.1 per cent) of those with initial values for K within the normal range also showed clinical evidence of cardiovascular dysfunction.

The one patient with low voltage QRS complexes in all three leads during the control period developed an increase to normal voltage before discharge.

Additional electrocardiograms were made before discharge in 15 of the 25 cases in which the T-wave had been inverted in one or more leads when the first tracing was taken; in 11 of these the T-wave had regained the upright position. This group included the 3 patients with inversion of the T-waves in all three leads and the 2 who showed an initial inversion of the T-waves in Leads II and III. Of the 4 patients who showed no change, 3 had had inverted T-waves in Lead III alone, and the fourth an inverted T-wave in Lead I with a diphasic T-wave in Lead II. None of these patients received digitalis.

Four of the 6 patients who had shown initial low voltage T-waves in all three leads had electrocardiograms again before discharge, and in 3 there was a return to normal voltage.

The depression of the S-T segment which had been present initially in 10 patients disappeared in each case after treatment.

All 3 patients who had right axis deviation on admission lost it before they were discharged. Electrocardiograms were repeated before discharge in 7 of the 16 cases of left axis deviation, and in 3 of these there was no abnormal deviation of the electrical axis.

In no case in which there was edema on admission was the serum albumin below 2.5 gm. per cent, or the total serum protein below 5 gm. per cent. The average total serum protein was 6.24 gm. and the average albumin-globulin ratio 3.77 : 2.47. These figures are slightly lower than the average for the entire group of subjects with complications.

Some degree of anemia was present in 13 of the 20 patients who had edema on admission, which is an incidence of 65 per cent, whereas the incidence of anemia in the "complicated" group as a whole was 72.4 per cent.

TABLE III

A COMPARISON OF THE CARDIOVASCULAR STATUS OF THE "UNCOMPLICATED" GROUP WITH THE "COMPLICATED" GROUP DURING THE CONTROL PERIOD

	UNCOMPLICATED	COMPLICATED
No of cases: Male	13 } 18	47 } 65
Female	5 }	18 }
Extremes in age	28—49	27—51
Average age	38	40
Previous heart disease	0	0
Cardiovascular symptoms	0	19 (29%)
Edema	0	20 (30.7%)
Palpable liver	0	26 (40%)
Average heart rate	88	101
Cardiac murmurs	0	9 (13.8%)
Enlarged heart (x-ray)	0 (out of 15)	14 (out of 55 = 25.4%)
Average blood pressure	134/84	136/87
Extremes of K: Male	0.3745—0.4318	0.3500—0.6306
Female	0.3946—0.4341	0.4041—0.5181
Average K: Male	0.4021	0.4323
Female	0.4107	0.4390
Low voltage of QRS in all 3 leads	1 (5.5%)	1 (1.5%)
Low voltage of T-waves in all 3 leads	1 (5.5%)	6 (9.2%)
Inverted T-waves		
in Lead I	0	1
in Lead III	3 (22%)	19 (47.7%)
in Leads II and III	0	2
in all 3 leads	0	3
Depressed S-T segments		
in Leads I and II	0	1
in Lead II	1 (5.5%)	1 (15.4%)
in Leads II and III	0	8
Right axis deviation	0	3 (4.6%)
Left axis deviation	1 (5.5%)	16 (24.6%)
Average plasma protein	6.52	6.32
Albumin	4.18	3.82
Globulin	2.34	2.5
Anemia		
Mild	2	12
Moderate	0 (out of 17)	21 (out of 58)
Severe	0 (11.7%)	9 (72.4%)

We were unable to correlate the variations in blood pressure readings of the patients with complications with the presence or absence of

anemia. Those without anemia had an average blood pressure of 144/94; those with a mild or moderate degree of anemia averaged 145/91; and those with a severe degree of anemia averaged 142/93. The range in blood pressure was practically the same in all groups.

The results by the second method of study are summarized in Table III. The preponderance of signs and symptoms of cardiovascular dysfunction in the complicated cases, as compared with the uncomplicated cases, is obvious. Nineteen patients in the "complicated" group had dyspnea, palpitation, precordial pain, or peripheral cyanosis on admission; 20 had pitting edema; and 25 had enlarged, palpable livers, whereas no patient in the "uncomplicated" group presented any of these signs. A comparison of the electrocardiograms shows a much greater incidence of inverted T-waves and depressed S-T segments in the complicated cases than in the uncomplicated cases.

In 20 subjects in the group with complications the relation of ventricular systole to the entire cardiac cycle was prolonged beyond the normal limits. No patient in the group without complications showed an abnormally large K. The patients in the "complicated" group revealed a higher incidence of tachycardia, and a greater incidence and severity of anemia, but there was no significant difference in the plasma protein levels of the two groups.

COMMENT

All the subjects of this study were alcohol addicts, but clinical evidences of cardiovascular dysfunction were found only among those patients who had one or more of the complications listed in Table I. It would appear, then, that alcohol per se is probably not the cause of the cardiovascular disturbances which occur in the alcohol addict. Of the 65 patients in the group with complications, 61 had polyneuritis on admission. There is abundant evidence to indicate that the primary etiologic factor in the polyneuritis of the alcohol addict is vitamin B_1 deficiency.[1-5] Of the four patients who showed no definite clinical signs of polyneuritis, two appeared to have the Korsakoff syndrome. The relatives of one of these patients said that he had eaten only one meal daily during the past year, and the other, who had had a posterior gastroenterostomy performed nine months before, had eaten irregularly for the preceding four months. Of the remaining two patients, one complained of a poor appetite of several months' duration, with persistent vomiting during the week immediately preceding; and the other admitted imbibing one quart of whisky daily for the past year, with irregular meals consisting of soup and sandwiches during the three weeks prior to admission. It is obvious that definite and severe dietary deficiencies were present in all of these 65 complicated cases.

The onset of symptoms referable to cardiovascular dysfunction was acute or subacute in every case, occurring from two days to two weeks

before admission, and the symptoms were progressive. When palpitation, dyspnea, and precordial pain occurred, they were usually the first signs to be noted by the patient. In addition to one or more of the above, a typical patient presented the following: Dependent edema, tachycardia, elevated systolic blood pressure, a palpable liver, a moderate degree of anemia, slight cardiac enlargement, a systolic murmur, and electrocardiographic abnormalities such as depression of the S-T segments, inverted T-waves, and prolongation of the constant K of Cheer and Dieuaide.[11]

In several instances it was observed that the degree of edema appeared out of proportion to the amount of demonstrable cardiac disease. In two subjects with extensive edema there were no signs or symptoms of cardiac embarrassment. The venous pressure was measured in one of these cases and found to be within normal limits.

The patients with signs and symptoms of cardiovascular dysfunction tended to improve when nothing was done except to keep them in bed on the basal[4] diet, but improvement was hastened in every case when the vitamin-rich diet was substituted for the vitamin-poor diet, and in four cases no improvement whatever was observed until after a high vitamin regimen had been instituted.

As these patients had been on diets deficient in a multiplicity of necessary food elements and were treated with diets rich in protein, fats, carbohydrates, and all the vitamins, it is difficult to say that any one of these factors was responsible for the disease or its cure.

It is well known that prolonged and severe deficiency of protein in the diet may cause considerable edema and many signs of cardiovascular dysfunction. However, in this series of cases, although the average serum protein level in the group presenting edema was somewhat lower than the average of the entire group, no patient had a total serum protein level below 5 gm. per cent, or a serum albumin below 2.5 gm. per cent. The range in values for total serum proteins and albumin fractions was as great in those who had edema as in those who did not.

Of the patients in the group with complications, 72.4 per cent presented some degree of anemia. A careful analysis of the figures, however, fails to reveal any correlation between the severity of the anemia and the number or severity of signs of cardiovascular dysfunction, including edema. As a matter of fact, several patients with severe edema and other signs of cardiovascular disturbance had no anemia.

The part played by a deficiency in the fat-soluble vitamins A and D in the production of these disturbances is probably negligible. First, these patients presented none of the well-recognized clinical evidences of deficiency in either vitamin A or D. Second, these vitamins are well stored in the body, and patients whose diets are deficient in all respects may therefore be expected to present signs of deficiency in one or more of the water-soluble vitamins long before evidences of vitamin A or D

deficiency are discernible. Platt and Lu[13] point out that "in high degrees of vitamin B_1 deficiency, signs of vitamin A deficiency are not seen except occasionally in minor forms, and when there are marked evidences of vitamin A deficiency, the manifestations of vitamin B_1 lack are submaximal." As indicated above, 61 of our patients showed definite evidences of vitamin B_1 deficiency. In studying the effects of the various vitamin deficiencies upon the electrocardiogram of the rat, Drury, Harris, and Maudsley[14] found that "of the vitamin deficiencies tested, A and D, separately and combined, appear to exert no characteristic influence upon the rhythm of or the conduction in the heart or upon the T-waves."

Only one of the 65 patients in the group with complications showed clinical evidence of scurvy. This individual had, in addition, a severe degree of peripheral neuritis.

The part played by vitamin B_2 (vitamin B_2 signifying the entire vitamin B complex minus B_1) in the production of both peripheral neuritis and cardiovascular disturbances in the alcohol addict is questionable. In an electrocardiographic study of 38 cases of pellagra, Feil[12] reports changes similar to those found in beriberi and in this study. Thirty-seven of his patients were alcohol addicts, and one was the victim of partial starvation. He reports that all of his patients had "the typical picture of pellagra with cutaneous, gastrointestinal and neurological symptoms of varying degree."

It is important here to point out that the neurologic symptoms occurring in alcohol addicts with pellagra are frequently seen in alcohol addicts who present none of the cutaneous, gastrointestinal, or mucous membrane lesions of pellagra. By far the most common of these neurologic manifestations in both groups is peripheral neuritis. The relationship of vitamin B_1 deficiency to the neuritis of the alcohol addict has been adequately demonstrated.[1-5] As the diet in Feil's cases was deficient in both vitamin B_1 and vitamin B_2, as all of his patients presented neurologic symptoms which from our studies[3, 4, 5] appear to bear a closer relationship to vitamin B_1 deficiency than to pellagra,* and finally, as his findings were similar to those reported in endemic beriberi, it is probable that the cardiac symptoms reported by him were in fact manifestations of vitamin B_1 deficiency. Porter and Higginbotham,[15] in a study of 25 selected cases of endemic pellagra, concluded that: "(1) The clinical evidence and necropsy studies show that the hearts of endemic pellagrins are normal or subnormal in size. (2) There are no characteristic electrocardiographic changes in endemic pellagra. Those changes that do occur are invariably explained by vascular or toxic complications. (3) Beriberi and pellagra have no comparable

*Since the submission of this paper for publication T. D. Spies and C. D. Aring (The Effect of Vitamin B_1 on the Peripheral Neuritis of Pellagra, J. A. M. A. 110: 1081, 1938) have confirmed this observation that the peripheral neuritis in pellagrins is primarily a manifestation of vitamin B_1 deficiency.

effect on the heart. The difference is so absolute that one ventures the opinion that B_1 is not concerned with the pathogenesis of pellagra."

That cardiovascular disturbances occur in beriberi is well known. This disease is frequently classified as follows: (1) the neuritic type, (2) the edematous type, (3) the mixed type, and (4) the cardiac type.[16] The similarity between the manifestations of cardiovascular dysfunction described in endemic beriberi[13, 16-20] and those presented in this study is striking. Indeed, our cases can be fitted accurately into the above classification of endemic beriberi.

Weiss and Wilkins[21] studied the nature of the cardiovascular disturbances in vitamin deficiency states in 97 patients admitted to Boston City Hospital, a large proportion of whom were alcohol addicts. In general, their findings agree with those of this study. They noted that in "patients with cardiac dilatation, peripheral arterial sounds, rapid peripheral flow and engorged veins occurred, but other patients with an identical type of deficiency showed pulmonary engorgement and the picture of left-sided failure." In some cases there was fatal collapse of the peripheral circulation simulating shock. We have already noted the protean nature of the cardiovascular disturbances which occur in alcohol addicts, and their similarity to those of endemic beriberi.

It is of interest here to point out that although right-sided enlargement of the heart is generally stressed in textbook discussions of beriberi heart disease, left-sided preponderance and diffuse enlargement frequently occur. There may be no notable change in the size or shape of the heart. Keefer[16] points out that pure right-sided dilatation is not an essential manifestation of beriberi heart disease. Scott and Herrmann,[17] in a study of eight cases of beriberi in Louisiana, reported a moderate enlargement of the heart in only two cases and a slight to moderate left ventricular predominance in electrocardiographic studies in every case. In this study we did not observe pure right-sided dilatation by roentgenographic examination, though in two instances there was a marked diffuse dilatation of the heart with right-sided predominance. Right deviation of the electrical axis on the initial electrocardiogram was observed in only three subjects, whereas left deviation occurred in 16.

In England Campbell and Allison[22] have reported a series of eight cases of polyneuritis, in which the symptoms of cardiovascular dysfunction were more prominent than the neuritic signs. They made the following interesting observation: "The type of polyneuritis in which cardiac changes occur most prominently is beriberi. The cases described here bear some resemblance to the milder types of the disease as it is described in the East. Had these cases been seen in the Orient, it is not improbable that they would have been attributed to that cause. On the other hand, it is open to question whether the varied diet of the European could ever become so deficient in vitamin B as to give rise

to polyneuritis with cardiac changes." The last statement in this quotation is open to considerable question.

That beriberi is a manifestation of avitaminosis (B_1) is so well-recognized that further discussion is unnecessary. As pointed out by Weiss and Wilkins,[21] "so far as is known at present, deficiency of vitamin B_1 is the only vitamin deficiency which is followed by disturbed function of the heart." Carter and Drury,[23] working experimentally with pigeons, and Drury, Harris, and Maudsley,[14] working with rats, demonstrated changes in cardiac rate when these animals were kept on diets deficient in vitamin B_1.

Edema is not as a rule observed in experimental animals whose diet is deficient in vitamin B_1, although Peters[24] has shown that when salt solution is given to these animals their weight may increase as much as 50 per cent. This edema may be completely dispelled by giving small amounts of vitamin B_1.

Peters[25] has demonstrated that there is an accumulation of lactic acid in the nervous tissue of pigeons fed with diets deficient in vitamin B_1. He was unable to demonstrate any toxic substance, or to produce symptoms in normal birds by the injection of lactate. An accumulation of abnormal quantities of lactic acid in the blood stream has also been demonstrated in patients with endemic beriberi by Inawashiro and Hayasaka.[26] This has been advanced to explain the facts that beriberi patients easily accumulate a large oxygen debt and require an abnormally long time to repay it and that severe cardiovascular dysfunction occurs in those who, because their peripheral neuritis is comparatively slight, are most capable of muscular exertion, and to account for the peculiar edema of muscle and other tissue which is not of cardiac origin.

Inawashiro and Hayasaka[26] point out that "if in patients with beriberi the acidotic condition of the muscle caused by contraction becomes very marked, the blood vessels in the muscle will become contracted, which makes the blood flow slow and in turn magnifies the acidosis in the muscle, the lactic acid resynthesis being further disturbed. Thus in the patients of beriberi an important cause has been brought forward of a swelling as well as claw pain of muscle." This may be applied to cardiac as well as to skeletal muscle, and may account for the anginal pain noted in three of the subjects of this study.

The incomplete oxidation of carbohydrate associated with the accumulation of abnormally large quantities of lactic acid in the blood and other tissues of subjects with vitamin B_1 deficiency may be the cause of the high systolic blood pressure frequently observed in subjects with beriberi at the acme of the disease. The occurrence of an elevated systolic blood pressure was observed by Weiss and Wilkins[27] in their study of vitamin deficiency states, and by us in this study. Lambert and Gellhorn[28] have demonstrated that the rise of blood pressure caused by

oxygen deficiency is greatly augmented by small amounts of carbon dioxide which in themselves have no effect upon blood pressure.

Of the 65 patients with complications included in this study, 26 presented large livers on admission. In 10 instances this enlargement was not associated with other clinical signs or symptoms of cardiovascular dysfunction. Vitamin therapy was followed by a decrease in the size of the liver in 14 patients, 7 of whom were in this latter group. We are not prepared to state whether this hepatic enlargement was due to circulatory failure or to the fatty changes frequently noted at autopsy in the livers of alcohol addicts.

SUMMARY AND CONCLUSIONS

Of 83 alcohol addicts who presented no evidence, past or present, of chronic cardiovascular or acute or chronic kidney disease, 18 showed none of the stigmas of alcohol addiction or deficiency disease. The evidence of cardiovascular disturbances in this group without complications was minimal. Of the remaining 65 patients, 61 had peripheral neuritis, 2 had alcoholic encephalopathy without neuritis, and 2 had portal cirrhosis without neuritis. Twelve patients had both neuritis and pellagra.

In this group of 65 patients with symptoms of dietary deficiency there was electrocardiographic evidence of cardiovascular disturbance in 47 per cent, and clinical evidence in 32.3 per cent. Ten additional patients presented large palpable livers without other demonstrable evidence of circulatory failure. The problem of the relative rôles played by fatty infiltration and chronic passive congestion of the liver in the hepatomegaly of these 10 subjects was presented.

We have pointed out the close resemblance of the clinical picture presented by alcohol addicts with cardiovascular disturbances to the various types of endemic beriberi, and have discussed the part played by deficiency of various accessory food elements in the production of these disturbances.

In conclusion we feel that this study supports the belief that beriberi in all of its manifestations is found in alcohol addicts in this country. From the data here presented we cannot estimate the incidence of cardiovascular disturbances in alcohol addicts in general. Our studies indicate, however, that approximately one-third of the alcohol addicts who show vitamin B_1 deficiency in the form of peripheral neuritis present clinical evidence of some degree of cardiovascular dysfunction secondary to this deficiency.

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A STUDY OF MYOCARDIAL HYPERTROPHY OF UNCERTAIN ETIOLOGY, ASSOCIATED WITH CONGESTIVE HEART FAILURE

With Consideration of the Rôle of Antecedent Hypertension*

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THAT congestive heart failure, with rare exceptions, is failure of the hypertrophied heart, has been frequently demonstrated,[1-8] and is now widely accepted.[9-13] In the absence of deforming valvular disease, congenital cardiac defects, mechanical barriers in the pulmonary circulation, adherent pericardium, or diffuse inflammatory myocardial disease, cardiac hypertrophy is generally referred to systemic arterial hypertension. When there exists a reliable clinical record of elevated blood pressure, this opinion appears to be valid. May, however, the rôle of antecedent hypertension be invoked when it is not clinically apparent? Because the blood pressure in patients with essential hypertension may be permanently reduced as a result of myocardial infarction,[14] or undergo alterations of a spontaneous nature[10, 15] or as a result of congestive heart failure,[10, 15] normal values obtained during the course of clinical observation cannot be used to exclude the possibility of antecedent hypertension.

In the absence of clinically demonstrated hypertension in cases of congestive heart failure with myocardial hypertrophy, may morphologic evidence be used to determine the presence or absence of antecedent hypertension? Although myocardial hypertrophy, without obvious cause, is in itself often interpreted as evidence that hypertension existed during life,[5, 6, 10, 16-18] proof for this is lacking. Alterations in the arterioles, particularly those of the kidneys, have been the commonly utilized structural indication of the existence of hypertension. Their use for this purpose has limitations because of the uncertainty concerning their incidence. It is held by many,[15, 16, 19-24] and denied by others,[25-27] that sclerosis of the arterioles is a constant feature of essential hypertension. The problem is further complicated by the occasional occurrence of arteriolar sclerosis in apparently normal nonhypertensive individuals, and in them bears some relationship to age.[15, 19, 28-30]

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During a period of three years, 43 cases of congestive heart failure with predominant left ventricular hypertrophy of uncertain etiology have come to necropsy from the wards of the Third (New York University) Division of Bellevue Hospital. Valvular disease, congenital defects, syphilitic aortitis, adherent pericardium, and inflammatory myocardial disease were absent, and the available blood pressure readings were normal. It occurred to us that if antecedent systemic arterial hypertension played a significant rôle in the cardiac hypertrophy of these patients, they should exhibit an incidence of arteriolar sclerosis similar to that observed in known cases of essential hypertension, and considerably above that of nonhypertensive individuals of the same age period. This report represents a comparative study designed to test this proposition and embraces a consideration of other factors which might operate in the pathogenesis of cardiac hypertrophy.

SOURCES OF MATERIAL AND METHODS

The cases employed in this study represent successive necropsies during a three-year period, excluding patients with valvular disease of the heart, congenital cardiac defects, syphilitic aortitis, adherent pericardium, inflammatory myocardial disease, or cor pulmonale. All of the necropsies were performed or supervised by one or more of us, and the method of examination was constant. The hearts were detached from the ascending aorta from 3 to 5 cm. above the aortic ring, and weighed unfixed, devoid of blood or parietal pericardium. The coronary arteries were opened throughout their subepicardial course by coronary scissors, or by transverse serial sections at intervals of 3 to 4 mm., or both.

The vessels of the kidneys and adrenals were chosen for microscopic study. A minimum of two, and an average of four, sections of each organ, stained with hematoxylin and eosin after paraffin embedding, were studied. The sections were mixed, and examination was made and recorded without knowledge of the clinical history or of the necropsy findings.

The spleen was not utilized because physiologic arteriolar changes in this organ are extremely common. The pancreas was excluded because autolysis often produces alterations in the arterioles simulating arteriolar sclerosis. Other viscera show the lesion too infrequently to be useful in this study.

In the kidney sections the preglomerular arterioles were studied for evidence of subendothelial hyaline thickening, which was classified as severe when the majority were involved, as mild if 2 to 5 affected arterioles were found in a single section, as 1+ if only a single hyalinized arteriole was discovered in any section, and as absent if none was

TABLE I

RENAL AND ADRENAL ARTERIOLAR SCLEROSIS IN 269 NONHYPERTENSIVE SUBJECTS

DECADE	NO. OF CASES EXAMINED	PRESENT IN SOME DEGREE IN KIDNEYS OR ADRENALS		PRESENT AS 1+ IN KIDNEYS		PRESENT AS MILD OR SEVERE IN KIDNEYS		PRESENT AS MILD OR SEVERE IN ADRENALS		PRESENT AS MILD OR SEVERE IN KIDNEYS OR ADRENALS		ARTERIAL SCLEROSIS OF KIDNEYS	
		NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
3	22	1	4.5	1	4.5	0	0	0	0	0	0	0	0
4	39	6	15.5	3	7.8	2	5.1	3	7.8	3	7.8	3	7.8
5	58	17	29.3	11	18.9	4	6.9	6	10.3	8	13.7	12	20.6
6	70	24	34.3	12	17.1	9	12.8	10	14.2	13	18.5	27	38.5
7	44	20	45.4	12	27.2	5	11.3	12	27.2	14	31.8	21	47.7
8	29	17	58.6	4	13.7	11	37.9	8	27.5	14	48.2	20	68.9
9	7	4	57.1	1	14.2	3	42.8	2	28.5	3	42.8	5	71.4

encountered. Sclerosis of the interlobular and arcuate arteries was recorded as mild or severe, depending on the diffuseness of the lesion and the degree of reduction of the lumen. Alterations of the arterioles in the capsule or pericapsular areolar tissue of the adrenals were noted as mild or severe, corresponding to the diffuseness of subendothelial hyaline thickening.

Clinical data were obtained from the hospital charts and recorded without knowledge of the necropsy findings. The diagnosis of congestive heart failure was made on clinical evidence.[31]

INCIDENCE OF ARTERIOLAR SCLEROSIS IN NONHYPERTENSIVE SUBJECTS

This group comprises 269 cases in which there was no clinical evidence of heart disease, chronic anemia, or hyperthyroidism, and in which the systolic blood pressure was constantly below 150, and the diastolic below 90. The incidence of sclerosis of the arterioles and arteries increases with advancing age (Table I), mild or marked sclerosis of the renal arteries is from two to four times as common as comparable degrees of sclerosis of the afferent glomerular arterioles, and the latter vessels are affected in mild or severe degree with increasing frequency, reaching an incidence of 42.8 per cent in the ninth decade. The adrenal arterioles are involved slightly more frequently than the renal arterioles.

In this group the incidence of 1+ renal arteriolar sclerosis shows little variation with age and is similar to that observed in the groups to be described subsequently. This constancy indicates that such sparse alterations have no relationship either to age or hypertension and therefore are of no value. Moritz and Oldt[30] observed similar focal vascular alterations in various tissues but disregarded them in their classification of the severity of arteriolar sclerosis.

With the possibility in mind that those patients with mild or severe arteriolar disease might have had essential hypertension before they were observed clinically, their cardiac weights were studied. The average weight of the hearts in the 55 cases in which there was mild or severe renal or adrenal arteriolar sclerosis was computed and found to be 336 gm. for males and 300 gm. for females. Similar average weights were obtained in the 34 cases in which there was mild or severe sclerosis of the renal arterioles alone. These results agree essentially with the average heart weights for the group as a whole (327 gm. for males and 279 gm. for females). Further evidence that the alterations in the arterioles of the kidneys and adrenals in this group were not the result of arterial hypertension is found in the fact that in only 7 of the 55 cases of this group did the heart weight exceed 400 gm. for males and 350 gm. for females.

INCIDENCE OF ARTERIOLAR SCLEROSIS IN ESSENTIAL HYPERTENSION

This group consists of 154 cases of hypertension, with a systolic blood pressure above 150, and a diastolic blood pressure above 90. All instances of chronic glomerulonephritis, hydronephrosis, chronic pyelonephritis, and polycystic kidneys were excluded.

There were 96 males and 58 females. Table II reveals the distribution of these cases according to the cause of death. Congestive heart failure was the cause of death in 63, or 40.9 per cent. In 10 additional cases congestive heart failure occurred during the period of clinical observation, although it was not the primary cause of death.

TABLE II

CAUSE OF DEATH IN 154 CASES OF ESSENTIAL HYPERTENSION

CAUSE	NO. OF CASES	PER CENT
Congestive heart failure*	63	40.9
Coronary thrombosis with shock	2	1.3
Cerebral hemorrhage and cerebral arteriosclerosis	28	18.1
Uremia	13	8.4
Hypertensive encephalopathy	7	4.5
Acute infections	16	10.4
Others	25	16.2

*Includes 15 cases of coronary thrombosis.

In these 154 cases the average weight of the heart was 537 gm. for males and 455 gm. for females. In the 73 cases of congestive heart failure the average heart weight was 613 gm. for males and 463 gm. for females, contrasting with that of 461 gm. for males and 450 gm. for females who did not show congestive heart failure.

The incidence of arterial and arteriolar sclerosis in 144 cases of essential hypertension is recorded in Table III. The group has been subdivided to illustrate the differences between those patients who died of congestive heart failure (69 cases) and those in whom congestive heart failure, cerebral arterial disease, and uremia were absent (33 cases). This division was made in order to compare the incidence of arteriolar changes in patients who died in the end stage of their disease (congestive heart failure, uremia, cerebral vascular disease) and in those who died prematurely of unrelated causes, in whom the vascular alterations might have been aborted. Of the former, 57, or 82.5 per cent. showed moderate or severe renal arteriolar sclerosis, contrasted with 18, or 54.6 per cent, of the latter group.

INCIDENCE OF ARTERIOLAR SCLEROSIS IN CARDIAC HYPERTROPHY OF UNCERTAIN ETIOLOGY

Included in this group are 43 patients with congestive heart failure whose blood pressure did not exceed 150 systolic and 90 diastolic. In all but two, congestive heart failure was present at the time of death.

TABLE III

RENAL AND ADRENAL ARTERIOLAR SCLEROSIS IN 144 CASES OF ESSENTIAL HYPERTENSION

GROUP	PRESENT IN SOME DEGREE IN KIDNEYS OR ADRENALS		PRESENT AS 1+ IN KIDNEYS		PRESENT AS MILD OR SEVERE IN KIDNEYS		PRESENT AS MILD OR SEVERE IN ADRENALS		PRESENT AS MILD OR SEVERE IN KIDNEYS OR ADRENALS		ARTERIAL SCLEROSIS OF KIDNEYS	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Entire group of 144 cases	126	87.5	21	14.6	102	71.0	93	64.5	113	78.5	121	84.0
69 cases with C.H.F.*	66	95.8	8	11.6	57	82.5	55	79.7	63	91.4	66	95.8
33 cases not dying of C.H.F., C.A.,† uremia or hyp. enc.‡	25	75.8	7	21.2	18	54.6	13	39.4	22	66.7	21	63.6

*Congestive heart failure.
†Cerebral arteriosclerosis or hemorrhage.
‡Hypertensive encephalopathy.

Valvular deformities, congenital cardiac defects, adherent pericardium, syphilitic aortitis, and inflammatory myocardial disease were absent in this group as in the two preceding groups. The age and sex of these patients are recorded in Table IV.

TABLE IV

AGE AND SEX IN CASES OF MYOCARDIAL HYPERTROPHY OF UNCERTAIN ETIOLOGY

DECADE	MALES	FEMALES
3	0	1
4	2	0
5	4	2
6	8	1
7	14	1
8	6	2
9	2	0
Total	36	7
Ratio	5.1	1

The anatomical diagnosis of cardiac hypertrophy is based in 32 instances upon heart weight in excess of 400 gm. for males and 350 gm. for females in patients whose body weight did not exceed 170 lb. In 3 instances, though the weight of the heart was below 400 gm., it was considered hypertrophied in relation to body weight. In those patients who weighed more than 170 lb., the heart weight was 450 gm. or more (8 cases). The heart weights are charted in Table V and are compared with those of patients with essential hypertension who died of congestive heart failure. The average heart weight for the undetermined etiology group (males 520 gm., females 460 gm) is below that of the hypertensive group (males 613 gm., females 463 gm.).

TABLE V

HEART WEIGHT IN CASES OF CONGESTIVE HEART FAILURE AND MYOCARDIAL HYPERTROPHY

HEART WEIGHT	UNCERTAIN ETIOLOGY		HYPERTENSIVE	
	MALE	FEMALE	MALE	FEMALE
300-349		1		3
350-399	1	1		8
400-449	6	2	5	
450-499	9		3	5
500-549	6	2	5	5
550-599	5		4	1
600-649	6	1	14	4
650-699	1		4	1
700-749	2		6	
750-799			3	1
800-849			1	
850-899			1	
900-940			2	
Total	36	7	48	28
Average heart weight	520	460	613	463

Table VI illustrates the incidence of arterial and arteriolar sclerosis and, when compared with Table III, shows the differences between these patients and those with essential hypertension. Mild or severe sclerosis of the renal arterioles is less than half as frequent in this group (30.9 per cent) as in cases of essential hypertension with congestive heart failure (82.5 per cent). A similar difference is observed when the incidence of mild or severe renal and adrenal arteriolar sclerosis is compared in the two groups (45.3 per cent and 91.4 per cent, respectively). Fig. 1 illustrates the distribution by decades of arteriolar sclerosis of the kidneys in this group as compared with the foregoing groups.

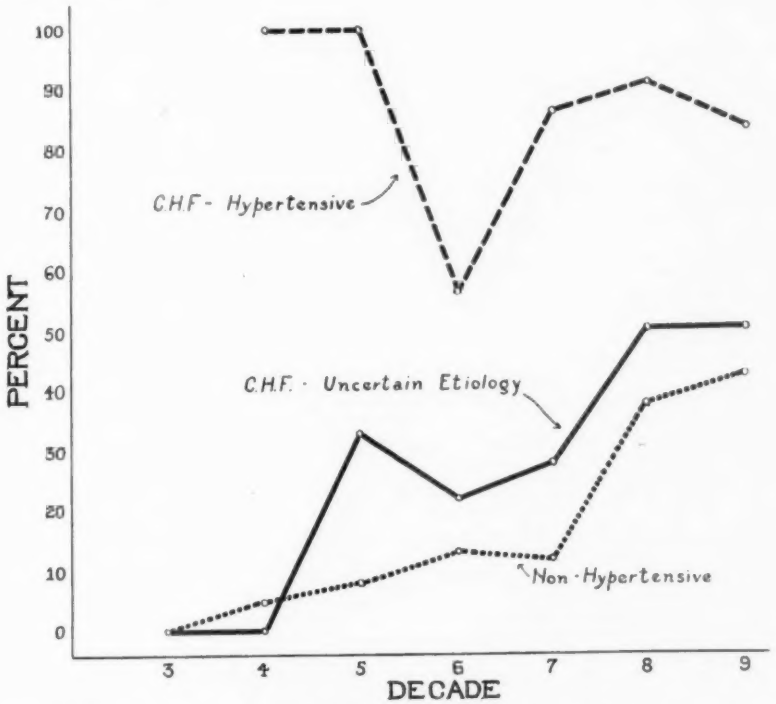

Fig. 1.—Relation of mild or severe renal arteriolar sclerosis to age. *C. H. F.*, congestive heart failure.

ANALYSIS OF DATA

It has been shown that mild or severe renal arteriolar sclerosis occurs in 12.6 per cent of nonhypertensive individuals and that in them its occurrence bears a definite relationship to age. These findings agree with those of Moritz and Oldt.[30] It is evident that subendothelial hyalinization of the renal arterioles in certain instances represents a senescent degenerative process which does not require for its production an abnormally elevated systemic arterial blood pressure.

TABLE VI

RENAL AND ADRENAL ARTERIOLAR SCLEROSIS IN 42 CASES OF MYOCARDIAL HYPERTROPHY OF UNCERTAIN ETIOLOGY

GROUP	PRESENT IN SOME DEGREE IN KIDNEYS OR ADRENALS		PRESENT AS 1+ IN KIDNEYS		PRESENT AS MILD OR SEVERE IN KIDNEYS		PRESENT AS MILD OR SEVERE IN ADRENALS		PRESENT AS MILD OR SEVERE IN KIDNEYS OR ADRENALS		ARTERIAL SCLEROSIS OF KIDNEYS	
	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%	NO.	%
Entire group of 42 cases	23	54.7	6	14.2	13	30.9	13	30.9	19	45.3	26	61.8
18 cases of myocardial infarction	12	66.7	3	16.6	7	38.9	8	44.4	10	55.6	13	72.3
24 remaining cases	11	45.8	3	12.4	6	25.0	5	20.8	9	37.5	13	54.2

The question of the constancy of arteriolar sclerosis in essential hypertension has played an important rôle in the search for the pathogenesis of that condition. Moritz and Oldt[30] found renal arteriolar sclerosis of significant degree in 97 of 100 cases of chronic hypertension and concluded "that renal arteriolar sclerosis is the most common cause of chronic hypertension." We encountered significant renal arteriolar sclerosis in 102 of 144 cases of essential hypertension, but, whereas Moritz and Oldt limited their study to patients with chronic hypertension dying in the end stage of the disease, our material included patients with hypertension in whom the natural course of the disease was interrupted by fatal intercurrent illness. That this variation in choice of material may be significant is revealed by the differences observed in the incidence of renal arteriolar sclerosis in our cases when a similar division is made. Arteriolar sclerosis was present in the kidneys of 82.5 per cent of patients with hypertension who died of congestive heart failure but was found in only 54.6 per cent of those who did not show evidence of congestive heart failure, uremia, or cerebral vascular disease.

The investigation of renal arteriolar sclerosis herein reported was designed to ascertain whether this vascular lesion could be utilized as a morphologic index of the existence of systemic arterial hypertension. Consideration of the pathogenesis of essential hypertension was not within the purpose of this study. The absence of subendothelial hyaline thickening of the renal arterioles in 45.5 per cent of cases of essential hypertension in which death occurred before the natural termination of the disease does not necessarily invalidate the rôle of renal ischemia in the genesis of chronic hypertension.[34] Of the 42 cases of essential hypertension in which there was no significant renal arteriolar sclerosis, sclerosis of the arcuate or interlobular arteries was found in 24. It is felt that in the remaining 18 cases the existence of

renal ischemia due to localized sclerosis of the larger branches of the renal arteries or their ostia cannot be excluded because of the limitations of examination.

As was pointed out earlier in this report, it was believed that, if arterial hypertension played a major rôle in the genesis of cardiac hypertrophy in the patients of the uncertain etiology group, then the incidence of renal arteriolar sclerosis in this group should be similar to that observed in known cases of essential hypertension. In the material analyzed, renal arteriolar sclerosis occurred in 82.5 per cent of patients with essential hypertension who died with congestive heart failure, but in only 30.9 per cent of those in the group of uncertain etiology. The age distribution of renal arteriolar sclerosis in the latter group is similar to that observed in nonhypertensive individuals (Fig. 1). Since a correlation exists between group incidence of sclerosis of the renal arterioles and chronic hypertension, the divergent frequency of this vascular lesion in these two groups suggests that they are also different in respect to the existence of arterial hypertension. Hence the deduction appears to be valid that hypertension did not play the same rôle in the cardiac hypertrophy of patients in the group of uncertain etiology as it did in the patients with essential hypertension. In respect to heart weight and sex distribution there are additional points of difference between the two groups (Table V).

It appears that there are no characteristics in common in these cases to permit identification as a unified group. Hence an effort was made to analyze further those factors which might operate in the production of cardiac hypertrophy.

FACTOR OF CORONARY SCLEROSIS

That coronary sclerosis may play a rôle in cardiac hypertrophy has been asserted by some[2, 9, 36, 37] and denied by others.[3, 5, 16, 35] The degree of coronary sclerosis was determined in the group of patients with cardiac hypertrophy of uncertain etiology and graded as + if there was atherosclerosis without reduction in the lumen, as ++ if there was slight reduction in the lumen, and as +++ if there was partial or complete occlusion of the lumen because of atherosclerosis or thrombosis.

In 19, or 44.2 per cent of the cases of uncertain etiology, coronary sclerosis was absent or recorded as + and cannot be considered as a factor in the production of myocardial hypertrophy, for this degree of coronary sclerosis is almost constant in persons in the fifth and later decades of life who exhibit neither clinical nor necropsy evidence of heart disease. In the remaining 24 cases (55.8 per cent), there was ++ or +++ coronary sclerosis, but, since myocardial infarction was present in 16 of these, coronary sclerosis per se could have played a

rôle in myocardial hypertrophy in only 8. In 4 of the latter other factors demand consideration (Table VII).

TABLE VII

POSSIBLE ETIOLOGIC FACTORS IN 43 CASES OF CARDIAC HYPERTROPHY OF UNCERTAIN ETIOLOGY

FACTOR	NO. OF CASES	MILD OR SEVERE RENAL ARTERIOLAR SCLEROSIS		AVERAGE HEART WEIGHT		CORONARY SCLEROSIS NO. OF CASES	
		NO.	%	MALE	FEMALE	NONE OR +	++ OR +++
Myocardial infarct	18	7	38.9	536	340*	2	16
Auricular fibrillation	5	0		556	510*	4	1
Chronic anemia	2	0		435		1	1
Hyperthyroidism	2	1	50.0		510	1	1
Combination of anemia and infarct	1	1	100.0	590			1
Unknown	15	4	26.6	494	450†	11	4

*1 case
†3 cases

FACTOR OF MYOCARDIAL INFARCTION

Old or both old and recent myocardial infarcts were present in 18 cases of cardiac hypertrophy of uncertain etiology. That myocardial infarction may lead to cardiac hypertrophy has been asserted by many.[2, 6, 9, 17, 38, 39] However, that hypertrophy frequently does not appear following infarction of the myocardium has been our experience as well as that of Horine and Weiss.[20] In the period encompassed by this study, 11 instances of old organized myocardial infarcts in hearts of normal size were encountered.

Although it is clear that infarction of itself does not constantly result in cardiac hypertrophy, infarction which leads to cardiac dilatation may produce it.[12, 32, 37] However, the following consideration supports the view that many of the cases of myocardial infarction in the group of cardiac hypertrophy of uncertain etiology represent instances of antecedent hypertension. Renal arteriolar sclerosis of mild or severe degree was found in 7 of the 18 cases (Table VI), an incidence which is only slightly less than that found in a group of cases of known hypertension with myocardial infarction (10 of 20 cases).

It is thus apparent that, although some of the cases of myocardial infarction in this group represent instances of antecedent hypertension, the actual number of these is not determinable.

OTHER POSSIBLE ETIOLOGIC FACTORS

If the 18 cases of myocardial infarction are excluded from the group of uncertain etiology, there are 25 instances in which the cause of

myocardial hypertrophy remains to be established. Considered as a group, the possible rôle of antecedent hypertension finds little morphologic support, for mild or severe renal arteriolar sclerosis was present in only 6, or 25 per cent (Table VI), and all of these patients were in the seventh and eighth decades, a period in which there is a not uncommon natural occurrence of these vascular changes (Table I). The average heart weight in this group (506 gm. for males and 480 gm. for females) was also somewhat below that which obtained in the hypertensive group. Significant degrees of coronary sclerosis occurred in only 8, or 32 per cent. Myocardial lesions of inflammatory nature were not found, and fibrosis of the myocardium was absent or of insignificant degree.

In Table VII the group of uncertain etiology has been subdivided according to various factors which, either in themselves or in association with others, might have played a rôle in the genesis of hypertrophy.

There were 5 cases in which protracted auricular fibrillation might have contributed to the development of myocardial hypertrophy. Renal arteriolar sclerosis was absent in all, and in only 1 instance could significant coronary disease be invoked as an additional factor. In 1 case the known duration of this arrhythmia was thirteen years, in another it was ten years, and in a third it was five years. In the study reported by Brown[40] there were 9 cases of persistent auricular fibrillation and cardiac hypertrophy.

Evidence that chronic anemia may lead to cardiac hypertrophy has been advanced by several investigators.[41-44] There were two patients with chronic anemia in this group; neither had arteriolar lesions, but one had coronary sclerosis. Cardiac hypertrophy was slight (420 and 450 gm.), and may have been related to the existing anemia.

Hyperthyroidism was prominent in 2 cases of this group, and in 1 case it was of six years' duration. Mild renal arteriolar sclerosis and ++ coronary sclerosis was present in 1 case.

In 1 case the association of severe chronic anemia, myocardial infarction, and mild renal arteriolar sclerosis precludes the implication of any one factor.

There remain 15 cases in this group of uncertain etiology in which none of the above factors existed. The low incidence of renal arteriolar sclerosis and the comparatively slight degree of cardiac hypertrophy separate this group from that of essential hypertension with congestive heart failure. A significant degree of coronary narrowing occurred in 4 of these cases and might have played a rôle in cardiac hypertrophy.

Although it is conceded that myocardial hypertrophy may have been the result of congestive heart failure in these cases, the nature of

any myocardial defect which might have reduced the efficiency of the heart is obscure. No structural myocardial alteration which might have initiated this process has been demonstrated in these 15 cases. The myocardial lesions disclosed by histologic study are of no apparent significance; they were small, scattered, interstitial, fibrous foci similar to those encountered in any hypertrophied heart. Since it is believed that vitamin B deficiency may be related to congestive heart failure,[45, 46] the clinical records in these cases were examined for possible evidence of the existence of vitamin B deficiency, but none was found.

Levy and von Glahn[47] recently reported 10 patients with congestive heart failure in whom cardiac hypertrophy of obscure cause existed. Some of their cases are similar to those in our group in respect to the absence of significant myocardial alterations.

Finally, it must be admitted that there may have been one or several unknown morphologic or functional abnormalities which helped to produce cardiac hypertrophy in these cases. Although the rôle of antecedent hypertension cannot be excluded in the individual case, its absence in the majority of these cases appears probable. Until further evidence is forthcoming, such clinical terms as "hypertrophy due to previous hypertension" or "arteriosclerotic heart disease" in designation of such cases should be employed with caution.

SUMMARY

Forty-three cases of preponderant left ventricular hypertrophy of uncertain etiology, associated with congestive heart failure, have been analyzed. Valvular disease, congenital cardiac defects, syphilitic aortitis, adherent pericardium, and inflammatory myocardial disease were excluded, and the available blood pressure readings were normal.

The possible rôle of antecedent hypertension in the genesis of cardiac hypertrophy was tested by comparing the incidence of renal arteriolar sclerosis in this group of patients with that in 269 nonhypertensive subjects of similar age and in 69 patients with essential hypertension who died in congestive heart failure.

Renal arteriolar sclerosis occurred in 12.6 per cent of nonhypertensive patients and in them bears a relation to age. In patients with chronic hypertension who died in congestive heart failure, sclerosis of the renal arterioles was encountered in 82.5 per cent, whereas in 42 cases of cardiac hypertrophy of uncertain etiology the incidence of this lesion was only 30.9 per cent.

Evidence is presented which suggests that antecedent hypertension played a part in the development of cardiac hypertrophy in many of the 18 cases of myocardial infarction which are included in this group. Other possible factors in the cardiac hypertrophy, namely, coronary

sclerosis, protracted auricular fibrillation, chronic anemia, and hyperthyroidism, were found in 14 of the 43 cases of uncertain etiology. In the remaining 11, structural or functional abnormalities which might have initiated cardiac dilatation and hypertrophy were not apparent. It is felt that although the rôle of antecedent hypertension cannot be excluded in the individual case, its absence in the majority of these cases appears probable.

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ABNORMAL DISTRIBUTION OF THE SUPERFICIAL MUSCLE BUNDLES IN THE HUMAN HEART*

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IT HAS often been remarked that knowledge is incomplete until quantitative data are available. Thus, information regarding the human coronary artery distribution acquired more practical value when Spalteholz[1] and later Gross[2] and Barnes and Whitten[3] were able to show that in 80 per cent of hearts one type of distribution was found. In regard to the ventricular muscle bands certain questions have come to mind:

1. Are these muscle bands present in all human hearts?
2. Are they present in an entirely constant pattern in all human hearts?
3. Are they present in a recognizable pattern but in relatively different masses under certain conditions?
4. What physiologic implications are involved in answering the above questions?

Constancy of Presence.—The first question is easily answered. Among fifty human hearts dissected in this laboratory, *none* has been found in which the superficial and deep sinospirals and bulbospirals were not identifiable. This is in accord with the observations of previous investigators (see Robb[4] for bibliography comprising 65 references), none of whom mention ever having studied a heart in which the discrete ventricular muscle bands were absent. The conclusion is warranted that the individual ventricular muscle bands are identifiable in 100 per cent of cases.

Constancy of Pattern.—a. The constancy of the pattern in all human hearts is another matter, though there is a general similarity. Thus far, no heart has been examined by us which did not have a *superficial bulbospiral muscle* arising from some part of the left auriculoventricular ring and spiraling downward to the apex to penetrate and form the inferior (posterior) papillary muscle. The variability of pattern in this muscle is observed chiefly in the extent of its origin. In some cases there may be an origin from the auriculoventricular ring at the right side of the pulmonary artery. MacCallum[5] (p. 312, Figs. 3 and 16) considers the origin of this layer to be "almost entirely from the tendon of the conus." Mall[6] describes the origin as from "the conus, the left side of the aorta, and the left side of the left auriculoventricular ring" (Mall,[6] p. 219, Fig. 1A-A'). Fibers of origin from the aorta and the

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left side of the left auriculoventricular ring were found in 100 per cent of our specimens. In about 20 per cent there is no origin further to the right, and in less than 10 per cent of hearts does a portion of the superficial bulbospiral muscle extend completely around the conus to its tendon. The posterior border of the origin of this muscle in about 5 per cent of the cases is at the obtuse margin. In 80 to 90 per cent it is at the mid-point of the posterior curve of the left auriculoventricular ring, and in 5 per cent (or less) a few fibers attach to the posterior end of the ligament. The portion of the inferior (posterior or diaphragmatic) surface of the heart which is covered by this muscle varies with the extent of the posterior origin. It may cover the apical two-thirds of the left ventricle and one-third of the right (if the origin ends at the obtuse margin), or as much as the whole of the left ventricle and the apical half of the right if the fibers attach to the whole posterior curve of the left auriculoventricular ring. There is some variability in the width of the band which curves about to form the posterior horn at the apex (Mall,[6] Fig. 7 C, p. 237).

b. A *superficial sinospiral* muscle is present in all hearts examined. The origin of this muscle is also somewhat variable. In about 5 per cent of the hearts the origin may extend from the entire posterior curve of the left auriculoventricular ring as far as the obtuse margin; in 80 to 90 per cent it will reach only to the mid-point of the left posterior curve of the left auriculoventricular ring, and in another 5 per cent of cases will have its entire origin from the right auriculoventricular ring. According to the extent of the origin, this muscle may cover the basal (upper) third of the left ventricle posteriorly, or may be confined entirely to the basal portion of the right ventricle. Even more important than the posterior extent of origin of this muscle is its variability on the anterior surface of the heart. At present it seems statistically unjustifiable to place much stress upon the percentage of variability in the anterior inferior portion of this muscle, for these specimens are not random samples, but are mainly hearts known to be abnormal and, moreover, the variations are manifold. Among 50 hearts examined, 4 showed great variation in pattern. Fig. 1 portrays the typical sweep of the superficial sinospiral fibers downward and forward over the anterior wall of the right ventricle. They cross the anterior interventricular sulcus, where the band condenses to form the lower third (or less) of the anterior wall of the left ventricle and the anterior horn at the apex, and then penetrates to form the anterior papillary muscle. Fig. 2 shows how the direction of these fibers is altered from an oblique to an almost horizontal direction by a considerable degree of cardiac hypertrophy, predominantly left-sided. Figs. 3 and 4 show deficiencies in this layer with abnormal insertion under the superficial bulbospiral and lessened participation in the formation of the anterior horn and anterior papillary muscle. Where the superficial sinospiral is deficient in the apical

region, the deep sinospiral emerges from the septum and becomes part of the anterior surface and contributes to the anterior horn and the anterior papillary muscle. In the light of Bremer's description[7] of the formation of the ventricles as "aneurysmal out-pouchings," such alterations in surface pattern are explicable.

c. The *deep sinospiral* muscle is fairly constant in pattern. It is deficient in the presence of large ventricular septal defects and may appear at the surface or contribute to the anterior horn and anterior papillary muscle as described above.

d. No variation in pattern of the *deep bulbospiral* muscle has been noted in this laboratory. Mall described this muscle as forming a cuff about the base of the left ventricle and passing through the septum,

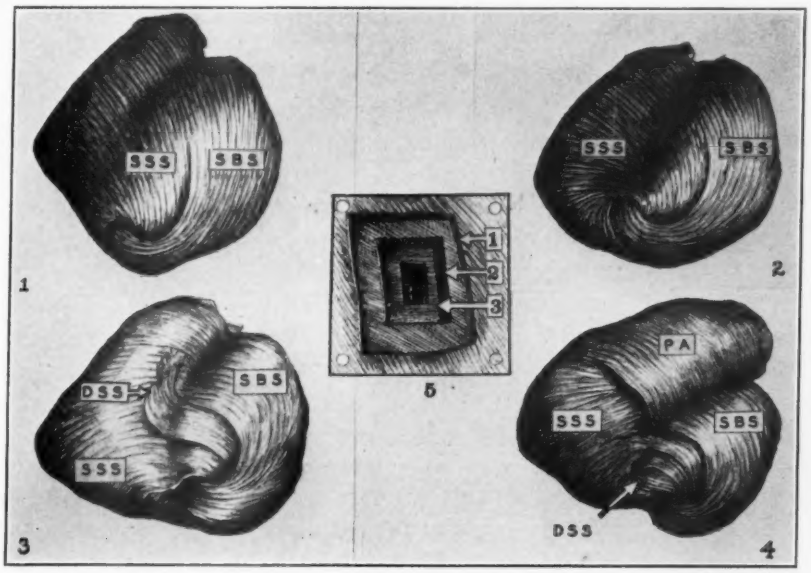

PLATE I.—Variations of superficial musculature in human hearts. (Anterior aspect, × ⅓.) Figs. 1-4 show anterior foreshortening due to tilting up of apex to exhibit the vortex. *SSS.* = superficial sinospiral muscle; *SBS.* = superficial bulbospiral; *DSS.* = deep sinospiral muscle; *PA.* = conus of pulmonary artery.

Fig. 1.—Normal, note oblique direction of *SSS* fibers.

Fig. 2.—Hypertrophy with more horizontal course of *SSS.* fibers.

Figs. 3 and 4 depict abnormal evagination of the deep sinospiral muscle fibers to the surface.

Fig. 5.—Window cut in lateral wall of left ventricle at the base showing relative thickness of muscle layers; arrows *1* = *SBS*, *2* = *DSS*, and *3* = *DBS* muscles, each layer characterized by different fiber direction (see Mall[6]).

but he did not emphasize the fact that it also encircled the aorta (Mall,[6] Figs. 9 and 11). Shaner[8c] finds that the deep bulbospiral surrounds both the aorta and the mitral orifice. This observation we have confirmed in human hearts.

Relation of Mass to Function.—Since these ventricular muscle bands are always present, we may inquire whether each has a specific function. W. G. MacCallum[9] writes (p. 451): "The arrangement of the musculature of the heart walls (J. B. MacCallum, Mall) is such as to control

TABLE I

LESION	THICKNESS IN MM. OF RIGHT VENTRICULAR WALL					THICKNESS IN MM. OF LEFT VENTRICULAR WALL						
	SSS	DSS	TOTAL	% TOTAL		SBS	DSS	DBS	TOTAL	% TOTAL		
				SSS	DSS					SSS	DBS	DSS
Normal*	1	3	4	25.0	75.0	1	3	6	10	10	30	60
1. Heart of small female. Normal valves. Coronary sclerosis.	0.75	2.25	3.0	25.0	75.0	1	2	4	7	14.5	29	57
2. Hypertrophy with hypertension. Valves normal.	1	3	4	25.0	75.0	1	6	9	16	7	37	56
3. Hypertension. Coronary sclerosis. Left ventricular hypertrophy.	1	3	4	25.0	75.0	1	5	15	25	4	20	76
4. Aortic stenosis.	1	4	5	20.0	80.0	1	5	11	17	6	29	65
5. Hypertension. Mitral stenosis. Coronary sclerosis. Old apical infarct.	1	6	7	14.5	85.5	1	3	13	17	6	18	76
6. Early mitral.	1	7	8	12.5	87.5	1	3	7	11	9	27	64
7. Moderate mitral stenosis + regurgitation. Moderate aortic stenosis + regurgitation. Early tricuspid.	1	8	9	11.1	88.9	1	3	9	13	8	23	69
8. Buttonhole mitral. Tricuspid regurgitation. Aortic stiffening.	1	6	7	14.3	85.7	1	3	3	7	14	43	43

*The figure of 4 mm. for the right ventricular wall and of 10 mm. for the left agrees with the upper limit of normals, without trabeculae, established by Nauwerck (quoted by Mallory and Wright[11]).

with greatest completeness the propulsion of blood; not only does it obliterate the cavity of the ventricles, but by the contraction of the papillary muscles it insures the proper tension and perfect closure of the auriculoventricular valves. Further, special subdivisions of the muscle support the semilunar valves and maintain their closure in such a way that even with slight imperfections of the valve leakage is much diminished by this muscular action."

This concept has been tested experimentally (Robb, Hiss, and Robb[10]). In brief, the two superficial muscles are responsible for little else than the fixing of the auriculoventricular valve leaflets during ventricular systole. Experimental injury has scarcely any effect on blood pressure. When the deep sinospiral contracts, it lessens all transverse diameters of the heart. It does all of the work of the right ventricle, and some of that of the left. Experimental injury will lower the blood pressure considerably, perhaps to half of its original value. The deep bulbospiral is responsible for the final emptying of the left ventricle and maintains systemic blood pressure at the end of systole. When this muscle relaxes, the aortic valves close. Experimental injury to this muscle causes a tremendous fall of blood pressure and often sudden death. If these experimentally observed functions prevail during life, various chronic lesions should lead to differential hypertrophy. Table I gives the measurements of the cross section of the muscles in the ventricular walls under various conditions, and Fig. 5 presents a sketch illustrating the method of obtaining the information.

It is readily seen (Table I) that in mitral disease the right portion of the deep sinospiral is hypertrophied. Normally this muscle comprises 75 per cent of the right ventricular wall. In mitral disease (e.g., Cases 5, 6, 7, 8) it formed 85 per cent, 87 per cent, 89 per cent and 86 per cent, respectively.

Normally the deep sinospiral forms about 30 per cent of the left ventricular wall at the base. In Case 2, showing general cardiac hypertrophy, this muscle increased its relative thickness to 37 per cent. Moreover, in a small heart (Case 8), in which both aortic and severe mitral disease were present, this muscle formed 43 per cent of the wall. When the work of the left ventricle is considerably increased, as in hypertension with hypertrophy (Case 3) and aortic stenosis (Case 4), the percentage of its mass was unchanged or even decreased though actually the muscle was thickened.

The deep bulbospiral normally forms about 60 per cent of the left lateral ventricular wall at the base. It is interesting to note that in Cases 3 and 5, in which hypertension was present, this muscle formed 76 per cent of the wall. In early uncomplicated mitral disease (Case 6) the deep bulbospiral was not significantly altered (normally 60 per cent of left wall, here 64 per cent), although the deep sinospiral on the right had increased in this heart from the normal of 75 to 87 per cent. In

a very small heart (Case 8) with very high-grade mitral disease, the deep bulbospiral formed less of the left wall than is normal and the deep sinospiral hypertrophied to 86 per cent on the right and 43 per cent on the left. Presumably in this case very inadequate filling of the left ventricle occurred, thus reducing the demand on the left ventricle. Variability in the deep bulbospiral was previously noted by Mall[6] (p. 247): "In the newborn and in young children this band is very insignificant, which indicates that during growth it must enlarge faster than the other heart muscle bundles. It also varies in size in the adult heart. Figs. 5 to 12 are taken from an hypertrophied heart which shows the circular bands markedly thickened. On the other hand, in a dilated heart with thin walls it is barely present, as Fig. 13 shows. To show further variations I add an illustration of a well-developed small heart in Fig. 14. Here the deep bulbospiral band is unusually well-developed, in fact as well as in the hypertrophied heart shown in Figs. 5 to 12."

In no instance of either hypertrophy or valvular lesion was there a measurable change in thickness of the surface layers of the superficial muscles. When mitral disease was advanced, the right papillary muscles tended to hypertrophy. In the most severe mitral lesion (Case 8), with reduction of the orifice to a small slit measuring only 7 by 1 mm. and calcification of the fused valve leaflets, the papillary muscles were atrophied. In the hypertensive hearts, and especially in the presence of aortic stenosis, the left papillary muscles were hypertrophied.

These findings substantiate the experimental conclusions regarding function. There is no doubt that differential hypertrophy of the ventricular muscle bands can and does occur in human hearts.

Physiological Implications.—Differences in surface pattern of the ventricular muscles offer a heretofore-unmentioned possibility of explaining the variable results of timing of initial negativity, of analyzing, localizing, and studying the contour of premature systoles, and of learning about the injury which may be inflicted by surgical exploration of the heart. It follows that if data are presented dealing with surface localization, an accurate sketch of the muscle arrangement should be provided (the fat and epicardium being first removed).

SUMMARY AND CONCLUSIONS

1. Fifty human hearts have been dissected to demonstrate the ventricular muscle bands.

2. The superficial and deep sinospiral and bulbospiral muscles were present in all hearts. We know of no report in which these muscles were said to be absent.

3. The surface pattern of these muscles, especially at the lower anterior surface of the right ventricle, at the right ventricle near the conus, along the trabeculated area, and at the anterior horn of the left

ventricle, is variable. The angle at which the superficial sinospiral muscle fibers pass from the anterior horn to the right base varies considerably. In small hearts the fibers have an oblique course, tending to approach the vertical from apex to base. In hypertrophied hearts these fibers have an almost horizontal course.

4. The masses vary considerably. The right portion of the deep sinospiral is differentially hypertrophied in mitral disease or in any other disease characterized by increased resistance to pulmonary blood flow. The deep bulbospiral is similarly hypertrophied in hypertension and aortic stenosis. If the work of the heart is much increased, the left portion of the deep sinospiral may also hypertrophy.

5. The surface portions of the two superficial muscles do not have a measurable variation in thickness. When intraventricular pressure is increased, the papillary portion of these superficial muscles hypertrophies. Conversely, in a heart with a "buttonhole" mitral opening and calcified leaves, the papillary muscles were atrophied.

6. If the surface muscles are variable in distribution, or if they are deficient, apparent discrepancies might occur when localizing points of initial negativity, the origin of premature beats, etc.

7. For surface localization of electrical phenomena, accurate sketches of the surface distribution of the cleaned muscle should be provided.

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THE EFFECT OF DIGITALIS ON THE FORM OF THE HUMAN ELECTROCARDIOGRAM, WITH SPECIAL REFERENCE TO CHANGES OCCURRING IN THE CHEST LEAD*

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IN 1913 Cohn and Fraser[1] observed inversion of the T-waves of the human electrocardiogram following the administration of digitalis. In a more detailed study two years later these authors together with Jamieson[2] described changes in the form of the T-waves and R-T segments of the three standard leads following the use of this drug. Since then other papers[3, 4, 5] relating to this subject have appeared.

Recently it has been shown that electrocardiograms derived from precordial leads may reveal early and characteristic changes in the presence of myocardial infarction.[6] We have found that digitalis also alters the form of the precordial electrocardiogram and that these changes may be confused with those resulting from coronary artery disease. There have appeared in the literature only a few brief references[7, 8, 9, 10] to these changes and only one short paper[11] devoted to them. In this report we shall describe the alterations which we have observed in the chest lead of the electrocardiogram following the administration of therapeutic amounts of digitalis.

PLAN OF OBSERVATION

There are thirty patients in whom the three standard leads as well as a chest lead were taken, not only before but also after the administration of therapeutic amounts of digitalis. All but five of them were in a basal metabolic state (Tables I and II) when the records were taken. With one exception (Case 30), the patients suffered from organic lesions of the cardiovascular system. The etiologic diagnosis was rheumatic fever in 17 patients, rheumatic fever and hypertension in 1,† hypertension in 4, hypertension secondary to chronic glomerular nephritis in 1,‡ arteriosclerosis in 4, and syphilis in 2. The examination of one patient who suffered from attacks of paroxysmal auricular flutter failed to reveal evidence of organic heart disease. Twenty-one patients exhibited no signs of congestive heart failure at the time these observations were made; the remaining nine were decompensated. Normal sinus rhythm was present in 27, and auricular fibrillation in the remaining 3 (Tables I and II). One patient (Case 19) exhibited intraventricular heart block (left bundle branch type, new terminology).

The preparation of dried digitalis leaves made and distributed by the American Heart Association§ was used. All patients received digitalis prepared from the

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†Included under the Rheumatic Group in Table I.

‡Included in the Hypertensive Group in Table II.

§0.1 gm. equivalent to one cat unit.

same batch. We found by experience that 1.8 gm. of this batch given within a period of twenty-four hours is an effective digitalizing amount.* It was the plan to give the digitalizing amount rapidly so that it might be absorbed within twenty-four hours after the initial dose. To this end 22 patients received 1.8 gm. of digitalis within a period of twenty hours. Of the eight other patients one† (Case 4) received 1.6 gm. within a period of eight hours; two (Cases 5 and 24), 1.7 gm. within twelve hours; one (Case 17), 1.9 gm. within thirteen hours; two (Cases 12 and 22), 1.8 gm. within twenty-three hours; one (Case 23), 2.0 gm. within twenty-eight hours; and one patient (Case 30) received 2.2 gm. within thirty hours. With but slight variation the method of digitalization was as follows: After a control record had been obtained, the patient was given 0.8 gm. of digitalis as the initial dose; this was followed four hours later by 0.5 gm. and then by 0.3 gm. and 0.2 gm. at four-hour intervals, making a total of 1.8 gm.

The chest lead was derived by placing the right arm electrode just within the apex and the left arm electrode in the left interscapular region. At the time the control record was taken, a mark was left on the chest wall at the site of the anterior electrode so that later records could be secured from the same area. This precordial derivation of the electrocardiogram in most normal adults is characterized by negative P-waves and T-waves and rather large diphasic Q-R complexes. The R-T segment is commonly depressed 1 to 2 mm. below the isoelectric line, and the T-wave varies between 6 and 10 mm. in depth. In making our observations, the standardization was such that one millivolt deflected the string 1 cm.; correction was not made for small errors in standardization. The time interval between the initial dose of digitalis and the first electrocardiogram after digitalization had been completed did not exceed thirty hours in 26 of the 30 cases (Tables I and II). Usually two or more records were taken after digitalization had been completed, and all but five patients received maintenance amounts of digitalis during the period of study.

OBSERVATIONS

Changes in the Three Standard Leads.—In every case changes in the form of the T-waves and R-T segments occurred in one or more of the three standard leads after therapeutic amounts of digitalis had been given. The cases‡ may be divided into three groups according to the changes which took place in the form of the T-waves. In the first group there are 18 patients (Cases 1, 2, 4, 6, 7, 9, 15, 16, 17, 18, 19, 21, 22, 24, 26, 28, 29 and 30). In these cases the T-wave decreased in its positive phase or increased in its negative phase in all three leads. In the second group, comprised of seven patients (Cases 3, 13, 14, 20, 23, 25, and 27), the T-wave increased in its positive phase in Lead I and decreased in its positive phase or increased in its negative phase in Lead III. The five patients remaining fall in a third group (Cases 5, 8, 10, 11, and 12). In these the T-wave remained unchanged in one of the leads and decreased in its positive phase or increased in its negative phase in the other two leads.

*Experience with this particular batch showed that, regardless of body weight, it was necessary to give this amount within twenty-four hours to slow the rapid ventricular rate in the presence of auricular fibrillation to about 70 per minute; it was considered the digitalizing amount.[12]

†Patient complained of slight nausea after 1.6 gm. were given.

‡In one of the patients (Case 23) the third lead was not obtained in the first record taken after digitalization had been completed; the next record, taken two days later, was used for comparison with the control (Table II).

TABLE I

THE EFFECT OF DIGITALIS ON THE FOUR-LEAD ELECTROCARDIOGRAM OF SUBJECTS SUFFERING FROM RHEUMATIC HEART DISEASE WITH AND WITHOUT CONGESTIVE HEART FAILURE

CASE AND HOSPITAL NUMBER	AGE (YR.)	*DIAGNOSIS	DATE	AMOUNT OF DIGITALIS GIVEN (GM.)	A-V CONDUCTION TIME (SEC.)	RATE PER MIN.	AXIS DEVIATION	SUMMARY OF CHANGES IN CHEST LEAD AFTER DIGITALIZING AMOUNT ONLY		TIME WITH REFERENCE TO INITIAL DOSE OF DIGITALIS
								R-T SEGMENT	T-WAVE	
Rheumatic Heart Disease Without Failure										
1†	28	M.S., and M.I., E. H.	10/ 8/34		0.17	107	right	Not changed	Negative to diphasic	Before 25 hr. after
J. S.		N.S.R.		1.8						
61475		Class I or IIa	10/10/34	0.3‡	0.18	80	right			
♀		Pregnancy 7 mo.	10/11/34	0.2	0.18	94	right			
			10/18/34	(daily)	0.19	97	right			
2†	28	M.S., and M.I., E.H.	10/20/34		0.18	94	none	Depressed to isoelectric	Negative to less negative	Before 25 hr. after
R. D.		N.S.R.		1.8						
68341		Class IIa	10/22/34	0.2	0.19	84	none			
♀		Pregnancy 5-6 mo.	10/30/34	(daily)	0.18	88	none			
3†	21	M.S., M.I., A.S. and A.I., E.H.	11/ 8/34		0.20	65	left	Not changed	Negative to less negative	Before 26 hr. after
E. P.		N.S.R.		1.8						
14505		Class IIa	11/10/34	0.2	0.20	61	left			
♂			11/13/34	(daily)	0.22	60	left			
			11/15/34		0.20	60	left			
4†	23	M.S. and M.I., E.H.	11/12/34		0.20	70	none	Not changed	Negative to less negative	Before 27 hr. after
A. G.		N.S.R.		1.6						
79037		Class I	11/14/34		0.20	65	none			
♂			11/17/34		0.22	59	none			
			1/10/35		0.22	70	none			

*In this table as well as in Table II, the following abbreviations are used:

The diagnoses in this paper conform to the nomenclature for cardiac diagnosis recommended by the Heart Committee of the New York Tuberculosis and Health Association, "Criteria for the Classification and Diagnosis of Heart Diseases," ed. 2, New York Tuberculosis and Health Association, New York, 1929.

M.S. = Mitral stenosis; *M.I.* = mitral insufficiency; *E.H.* = enlarged heart; *N.S.R.* = normal sinus rhythm; *A.S.* = aortic stenosis; *A.I.* = aortic insufficiency; *A.F.* = auricular fibrillation.

†Indicates patient was in a basal metabolic state at the time records were obtained.

‡In this case as well as in the subsequent cases maintenance amounts of digitalis were not given until after the first record following digitalization had been obtained.

TABLE I—CONT'D

5†	23	M.S., M.I. and A.I., E.H.	2/14/35		0.18	72	left	Not changed	Negative to	Before
A. M.		N.S.R.		1.7					less negative	27 hr. after
37709		Class I or IIa	2/16/35		0.18	60	left			
♀										
6†	19	M.S., M.I., A.I. and A.S., E.H.	3/18/35		0.18	71	none	Not changed	Negative to	Before
E. C.		N.S.R.		1.8					less negative	27 hr. after
33078		Class I	3/20/35		0.18	68	none			
♀			3/21/35		0.19	67	none			
7†	20	M.S., M. I. and A.I., E.H.	4/ 6/35		0.14	61	none	Not changed	Negative to	Before
R. L.		N.S.R.		1.8					less negative	29 hr. after
90113		Class IIa	4/ 8/35	0.3	0.15	75	none			
♂			4/ 9/35		0.15	62	none			
8†	24	M.S. and M.I., E.H.	4/13/35		0.18	75	right	Not changed	Diphasic to	Before
F. S.		N.S.R.		1.8					less negative	28 hr. after
89187		Class I	4/15/35		0.22	52	right			
♂			4/16/35		0.23	65	right			
			4/19/35		0.21	70	right			
9†	26	M.S., M.I., A.S. and A.I., E.H.	5/18/35		0.16	70	none	Isoelectric to	Negative to	Before
J. F.		N.S.R.		1.8				elevated	diphasic	28 hr. after
31027		Class I	5/20/35		0.16	52	none			
♀			5/21/35	0.2						
			5/22/35		0.16	70	none			
10	36	M.S., M.I. and A.I., E.H.	6/15/35		0.23	88	left	Not changed	Form	Before
H. K.		N.S.R.		1.8					changed	24 hr. after
96957		Class IIa	6/16/35		0.26	86	left		slightly	
♀			6/17/35		0.24 to 0.26	88	left			
11	37	M.S., M.I., A.S. and A.I., E.H.	9/18/35		0.16	125	right	Isoelectric to	Diphasic	Before
L. D.		N.S.R.		1.8				elevated	to positive	23 hr. after
98021		Class IIa	9/19/35		0.22	83	right			
♀		Pregnancy 6 mo.	9/20/35	0.1	0.22	91	right			
12	41	No valvular disease	9/17/35	1.8	0.14	100	left	Not changed	Negative to	Before
P. K.		Class F	9/18/35		0.16	94	left		less negative	28 hr. after
100918		Pregnancy 9 mo.	9/19/35	0.1	0.15	100	left			
♀			9/20/35	0.1	0.15	91	left			

TABLE I—CONT'D

CASE AND HOSPITAL NUMBER	AGE (YR.)	*DIAGNOSIS	DATE	AMOUNT OF DIGITALIS GIVEN (GM.)	A-V CONDUCTION TIME (SEC.)	RATE PER MIN.	AXIS DEVIATION	SUMMARY OF CHANGES IN CHEST LEAD AFTER DIGITALIZING AMOUNT ONLY		TIME WITH REFERENCE TO INITIAL DOSE OF DIGITALIS
								R-T SEGMENT	T-WAVE	
13† C. W. 88345 ♂	25	M.S. and M.I., E.H. N.S.R. Class I	12/19/35	1.8	0.22	60	right	Not changed	Positive to diphasic and decreased positive phase	Before 27 hr. after
			12/21/35	0.2	0.21	42	right			
			12/23/35	(daily)	0.22	60	right			
14† W. M. 126827 ♂	47	A.S. and A.I., E.H. N.S.R. Class IIa	3/30/36	1.8	0.16	71	none	Not changed	Diphasic to increased negative and positive phases and changed form	Before 26 hr. after
			4/ 1/36	0.2	0.17	88	none			
			4/ 2/36		0.16	73	none			
15 B. S. 147113 ♂	17	M.S., M.I., A.S. and A.I., E.H. N.S.R. Class IIa	11/27/36	1.8	0.20	88	none	Not changed	Negative to less negative	Before 26 hr. after
			11/28/36	0.1	0.20	81	none			
			11/30/36	(daily)	0.19	83	none			
Rheumatic Heart Disease With Failure										
16† M. C. 119155 ♀	53	M.S. and M.I., E.H. Hypertension A.F. Class IIb	1/28/36	1.8	A.F.	126	none	Not changed	Negative to less negative	Before 28 hr. after
			1/30/36	0.2	A.F.	80	none			
			2/ 1/36	(daily)	A.F.	90	none			
17† S. S. 123829 ♂	32	M.S., M.I. and A.I., E.H. N.S.R. Class IIb	2/19/36	1.9	0.26	75	right	Not changed	Negative to less negative	Before 27 hr. after
			2/21/36	0.2	0.30	56	right			
			2/24/36	(daily)	0.32	52	right			
18† G. Mac F. 124205 ♂	57	M.S. and M.I., E.H. A.F. Class IIb	2/25/36	1.8	A.F.	108	none	Isoelectric to elevated	Positive to increased amplitude	Before 29 hr. after
			2/27/36	0.2	A.F.	80	none			
			2/29/36	(daily)	A.F.	70	none			

In every case except two, the R-T segments became isoelectric, depressed, or more depressed in one or more of the three standard leads following digitalization. That is to say, there was a general tendency toward depression of the R-T segment in these cases. In the two exceptions mentioned above (Cases 3 and 20), however, isoelectric R-T segments in the third lead became elevated after digitalis. In those patients receiving maintenance amounts of digitalis, later records showed usually that the changes as already described in the T-waves and R-T segments became more marked; in a few instances, however, the T-waves varied only slightly (Tables I and II).

Changes in the Chest Lead.—Changes in the form of the chest lead were evident in the first record taken after digitalization in 29 of the 30 patients. These 29 patients fall into ten groups according to the changes which were observed in the form of the T-waves.

1. The case of A. G. (Case 4) serves to illustrate the change that occurred in 15 instances (Cases 2, 3, 4, 5, 6, 7, 12, 15, 16, 17, 21, 25, 26, 27 and 28) in which a negative T-wave became less negative (Fig. 1).

2. The case of J. F. (Case 9) serves to illustrate the change that occurred in three instances (Cases 1, 9 and 30) in which a negative T-wave became diphasic (Fig. 2).

3. The case of C. M. (Case 22) illustrates the change that occurred in one instance in which a negative T-wave became positive (Fig. 3).

4. The case of L. B. (Case 20) serves to illustrate the change that occurred in three instances (Cases 8, 20 and 23) in which a diphasic T-wave decreased in its negative phase, and, in one of these, increased in its positive phase also (Fig. 4).

5. The case of C. McA. (Case 24) illustrates the change that occurred in one instance in which a diphasic T-wave increased in its positive phase only (Fig. 5).

6. The case of L. D. (Case 11) illustrates the change that occurred in one instance in which a diphasic T-wave became positive (Fig. 6).

7. The case of G. MacF. (Case 18) illustrates the change that occurred in one instance in which a positive T-wave increased in amplitude (Fig. 7).

8. The case of C. W. (Case 13) serves to illustrate the change that occurred in two instances (Cases 13 and 29). In one of these (Case 13) a positive T-wave became diphasic and decreased in its positive phase (Fig. 8); in the other (Case 29) a diphasic T-wave became negative and increased in its negative phase.

9. In one instance (Case 14) a diphasic T-wave increased in both its positive and negative phases.

10. In one instance (Case 10) no change occurred in the amplitude of the T-wave, but its contour was altered.

In short, after the administration of therapeutic amounts of digitalis the T-wave in twenty-five cases (those cases included in the first seven

TABLE II

THE EFFECT OF DIGITALIS ON THE FOUR-LEAD ELECTROCARDIOGRAM OF PATIENTS SUFFERING FROM HYPERTENSIVE, ARTERIOSCLEROTIC AND SYPHILITIC HEART DISEASE WITH AND WITHOUT CONGESTIVE HEART FAILURE, AS WELL AS OF ONE NORMAL INDIVIDUAL

CASE AND HOSPITAL NUMBER	AGE (YR.)	DIAGNOSIS	DATE	AMOUNT OF DIGITALIS GIVEN (GM.)	A-V CONDUCTION TIME (SEC.)	RATE (PER MIN.)	AXIS DEVIATION	SUMMARY OF CHANGES IN CHEST LEAD AFTER DIGITALIZING AMOUNT ONLY		TIME WITH REFERENCE TO INITIAL DOSE OF DIGITALIS
								R-T SEGMENT	T-WAVE	
Hypertensive Heart Disease Without Failure										
19* A. G. 125389 ♀	62	Arteriosclerosis †L.I.—V. H-B.	3/11/36	1.8	0.16	77	left	Not changed	Not significantly changed	Before 26 hr. after
		N.S.R.	3/13/36	0.2	0.18	71	left			
		Class I	3/14/36		0.18	65	left			
Hypertensive Heart Disease With Failure										
20* L. B. 124739 ♂	64	Arteriosclerosis, E.H.	2/29/36	2.0	0.16	100	left	Not changed	Diphasic to decreased negative phase	Before 46 hr. after
		N.S.R.	3/ 2/36	0.2	0.18	64	left			
		Class IIb	3/ 6/36	(daily)	0.18	70	left			
21* E. R. 94711 ♂	44	Arteriosclerosis, E.H.	5/11/35	1.8	0.15	100	none	Not changed	Negative to less negative and changed form	Before 29 hr. after
		N.S.R. Class IIb	5/13/35		0.16	83	none			
22 C. M. 113159 ♂	34	Chronic Glomerular Nephritis	11/11/35	1.8	0.15	103	left	Depressed to isoelectric	Negative to positive	Before 41 hr. after
		Secondary Hypertension, E.H. N.S.R. Class III	11/13/35		0.16	83	left			
23* A. F. 118112 ♂	38	E.H.	1/ 4/36	2.0	0.16	94	left	Depressed to less depressed	Diphasic to decreased negative phase and increased positive phase	Before 46 hr. after
		N.S.R. Class III	1/ 6/36	0.2	0.16	73	left			
			1/ 8/36	(daily)	0.17	75	left			
			1/15/36		0.18	65	left			

*Indicates patient was in basal metabolic state when records were obtained.
†L.I.—V. H-B. = Intraventricular heart block (left bundle branch type (new terminology).

TABLE II—CONT'D

TABLE II—CONT'D

Arteriosclerotic Heart Disease Without Failure										
24* C. McA. 14258 ♂	68	Coronary Artery Disease, M.I. N.S.R. Class IIa	1/15/35	1.7	0.15	70	none	Isoelectric to elevated	Diphasic to reversed order of phases and increased positive phase	Before 26 hr. after
			1/17/35		0.15	75	none			
			1/19/35		0.16	70	none			
25* J. S. 109757 ♂	58	Coronary Artery Disease N.S.R. Class IIa	10/29/35	1.8	0.17	57	left	Depressed to isoelectric	Negative to less negative	Before 26 hr. after
			10/31/35		0.18	52	left			
			11/ 4/35	0.1-0.2	0.18	61	left			
			11/ 6/35	(daily)	0.18	60	left			
26* M. M. 123080 ♀	57	Coronary Artery Disease, E.H. A.F. Class IIa	2/15/36	1.8	A.F.	136	none	Isoelectric to elevated	Negative to less negative	Before 25 hr. after
			2/17/36	0.2-0.3	A.F.	95	none			
			2/21/36	(daily)	A.F.	90	none			
Arteriosclerotic Heart Disease With Failure										
27* C. K. 99561 ♂	48	Coronary Thrombosis N.S.R. Class IIb	11/13/35	1.8	0.16	111	none	Not changed	Negative to less negative and changed form	Before 26 hr. after
			11/15/35		0.20	105	none			
			11/18/35	0.2 (daily)	0.18	103	none			
Syphilitic Heart Disease Without Failure										
28* H. W. 71762 ♂	48	Syphilitic Aortitis A.I., E.H. N.S.R. Class I	10/17/34	1.8	0.16	66	none	Depressed to isoelectric	Negative to less negative	Before 26 hr. after
			10/19/34	0.2	0.18	61	none			
			10/23/34	(daily)	0.18	61	none			
			10/26/34		0.18	79	none			
Syphilitic Heart Disease With Failure										
29* J. K. 129406 ♂	55	Syphilitic Aortitis A.I., E.H. N.S.R. Class III	4/15/36	1.8	0.18	88	none	Depressed to more depressed	Diphasic to negative with increased negative phase and changed form also	Before 27 hr. after
			4/17/36		0.20-0.21	120	none			
			4/20/36		0.18	97	left			
Normal Heart										
30* H. B. 113637 ♂	21	No evidence of heart disease N.S.R.	12/18/35		0.15	65	none	Not changed	Negative to diphasic	3 wk. after stopping digitalis 66 hr. after
			11/26/35	1.0						
			11/27/35	1.2						
			11/29/35		0.15	91	none			

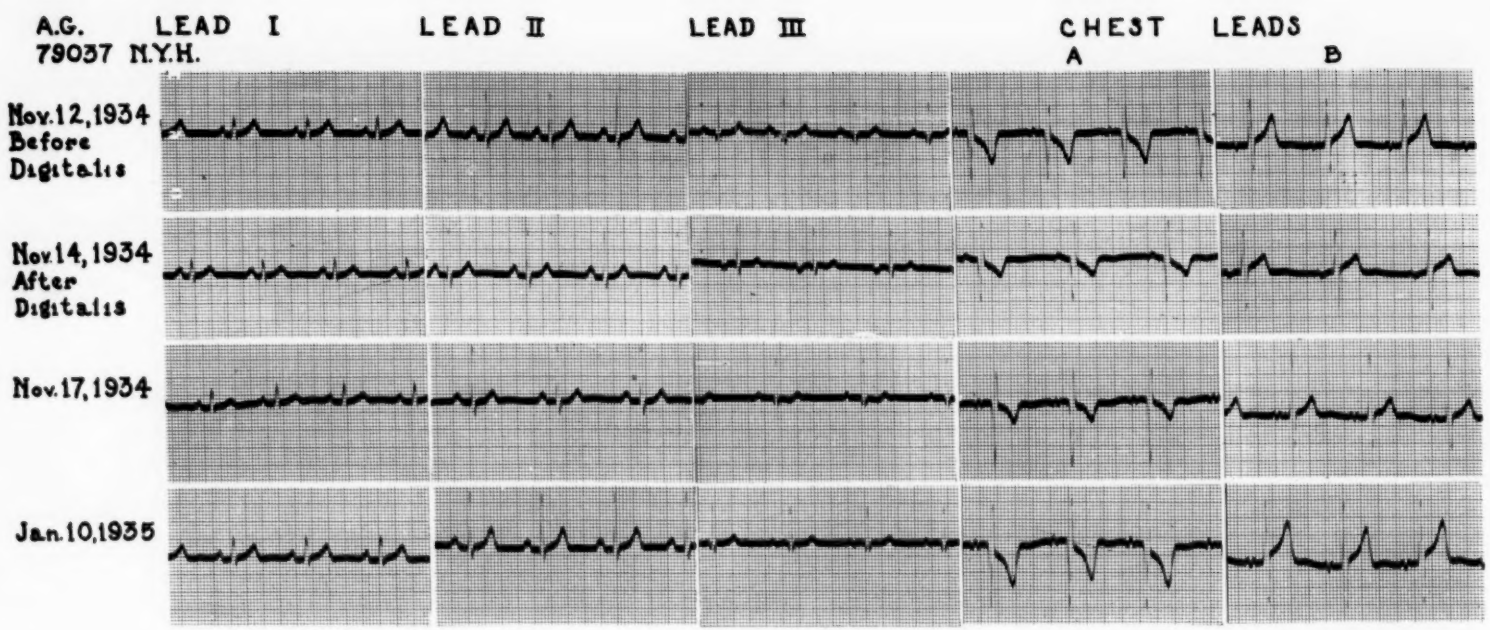

Fig. 1.—In this figure as well as in Figs. 2 to 8, inclusive, reproductions of the three standard leads and two chest leads are shown. Chest lead A is a reproduction of the original tracing (see text). In chest lead B the original film is printed so that the tracing is like that which would be derived by reversing the order of the electrodes on the chest, that is to say, from placing the left arm electrode anteriorly and the right arm electrode posteriorly. This was done so that the second chest lead would be comparable to the derivation to be recommended by the American Heart Association's Committee on Standardization of the Chest Lead.[13] The first tracing in each figure is the control record. The standardization in all records was such that 1 millivolt produced a 1 centimeter deflection of the string. Divisions of the ordinates equal 10^{-4} volt. Divisions of the abscissae equal 0.04 sec. The electrocardiograms in all figures are reduced to five-elevenths of their natural size. In this figure the electrocardiograms of A. G. (Case 4) are reproduced. The records in this case serve to illustrate the change that occurred in fifteen instances in which negative T-waves in the chest lead became less negative after digitalis. This patient received 1.6 gm. of digitalis between 6:00 A.M. and 6:00 P.M. on Nov. 13, 1934. In this case maintenance amounts of digitalis were not given, and the T-waves in the chest lead as well as in the three standard leads returned toward their original form.

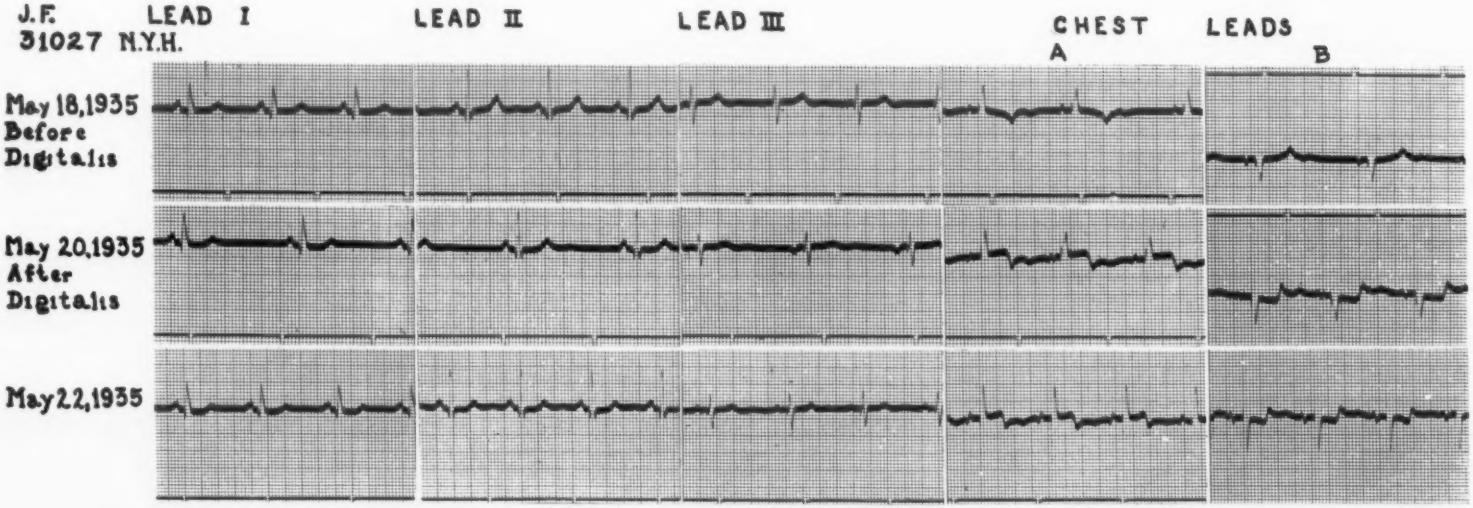

Fig. 2.—In this figure the electrocardiograms of J. F. (Case 9) are reproduced. The records in this case serve to illustrate the change that occurred in three instances in which negative T-waves in the chest lead became diphasic after the administration of digitalis. This patient received 1.8 gm. of digitalis between 6:00 A.M. and 6:00 P.M. on May 19, 1935, and 0.2 gm. additional on May 21, 1935.

groups above) became less negative, diphasic, or positive; if diphasic beforehand, it decreased in its negative phase or increased in its positive phase or exhibited both changes; if already positive, it increased in amplitude only. In two cases (included in Group 8) the reverse

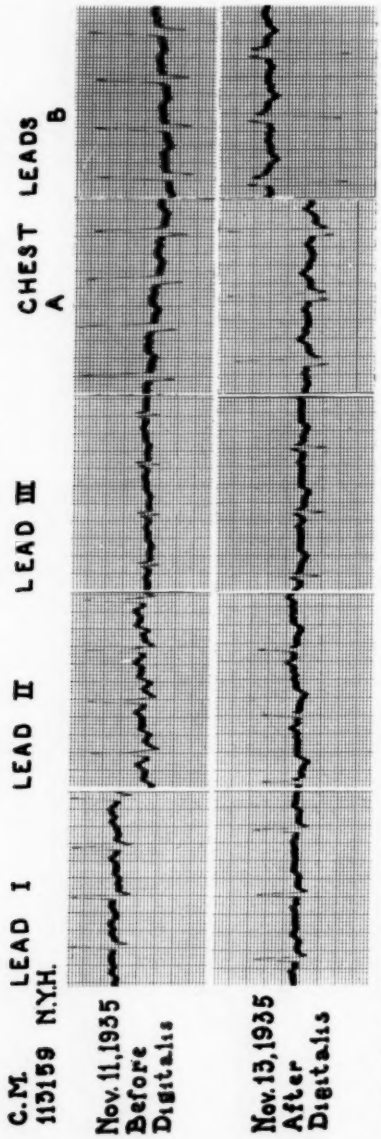

Fig. 3.—In this figure the electrocardiograms of C. M. (Case 22) are reproduced. The records in this case illustrate the change that occurred in one instance in which negative T-waves in the chest lead became positive after the administration of digitalis. This patient received 1.8 gm. of digitalis between 6:00 P.M. on Nov. 11, 1935, and 4:00 P.M. on Nov. 12, 1935.

change occurred, the T-wave decreasing in its positive phase and increasing in its negative phase. In the remaining two cases (Groups 9 and 10) the alterations were different still. In one (Case 10) of these, however, a negative T-wave became diphasic in a later record (Table I) thus placing it in the second group above.

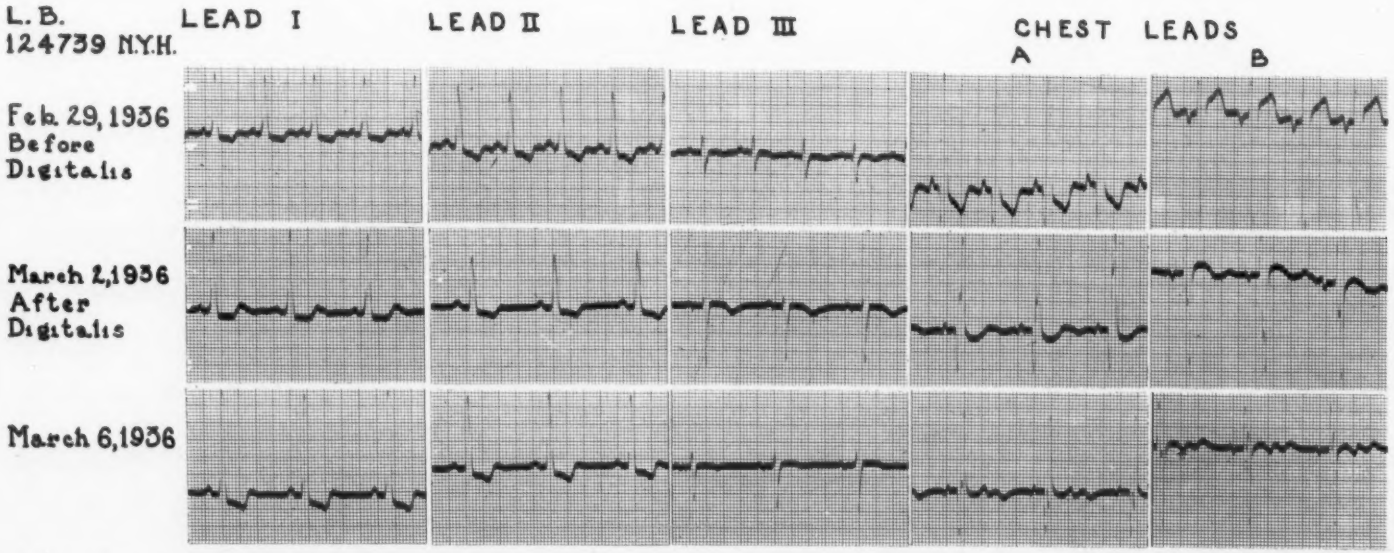

Fig. 4.—In this figure the electrocardiograms of L. B. (Case 20) are reproduced. The records in this case serve to illustrate the change that occurred in three instances in which diphasic T-waves in the chest lead decreased in their negative phase after the administration of digitalis. This patient received 2.0 gm. of digitalis between 12:00 M. on Feb. 29, 1936, and 4:00 P.M. on March 1, 1936. During the remainder of the period of study he received 0.2 gm. daily as a maintenance dose.

In one patient only (Case 19) did the form of the chest lead remain unchanged after digitalization. Twenty-four hours later, this patient

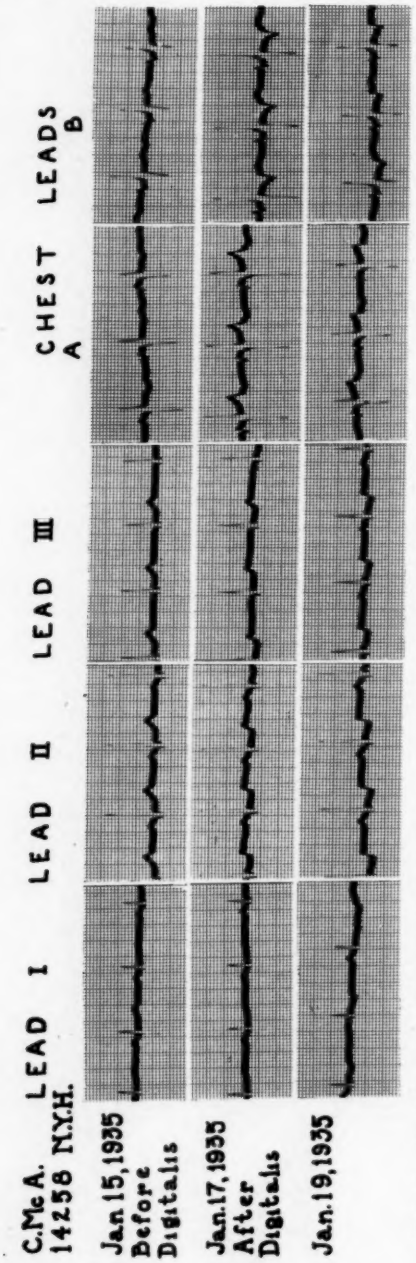

Fig. 5.—In this figure the electrocardiograms of C. McA. (Case 24) are reproduced. The records in this case illustrate the change that occurred in one instance in which diphasic T-waves in the chest lead increased in their positive phase only after the administration of digitalis. This patient received 1.7 gm. of digitalis between 9:00 A.M. and 9:00 P.M. on Jan. 16, 1935. Maintenance amounts of digitalis were not given to this patient.

having received 0.2 gm. of digitalis, the form of the T-waves and R-T segments was still unaltered. In this case the T-wave was positive, and the R-T segment isoelectric.

The changes in the R-T segments in the chest lead were not as marked as those in the T-waves. In nineteen cases no significant change was observed in this part of the electrocardiogram in the first record taken after digitalization had been completed. In ten patients (Cases 2, 9, 11, 18, 22, 23, 24, 25, 26 and 28) the R-T segment became

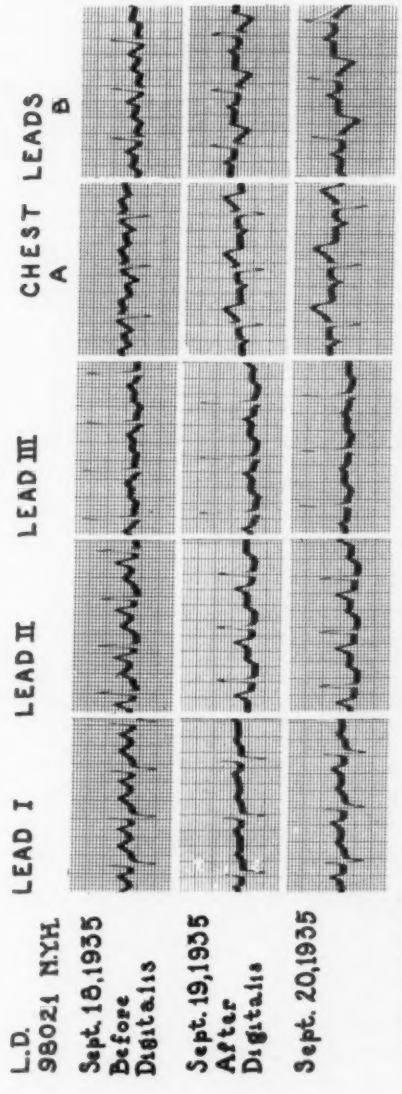

Fig. 6.—In this figure the electrocardiograms of L. D. (Case 11) are reproduced. The records in this case illustrate the change that occurred in one instance in which diphasic T-waves in the chest lead became positive after the administration of digitalis. This patient received 1.8 gm. of digitalis between 1:00 P.M. on Sept. 18, 1935, and 7:00 A.M. on Sept. 19, 1935, and 0.1 gm. additional on Sept. 20, 1935.

less depressed, isoelectric, or elevated; in short, there was a tendency toward elevation of the R-T segment in these cases. In one instance only (Case 29) did the R-T segment become more depressed after digitalis. In this case the T-wave which was diphasic before digitalis became negative and increased in its negative phase.

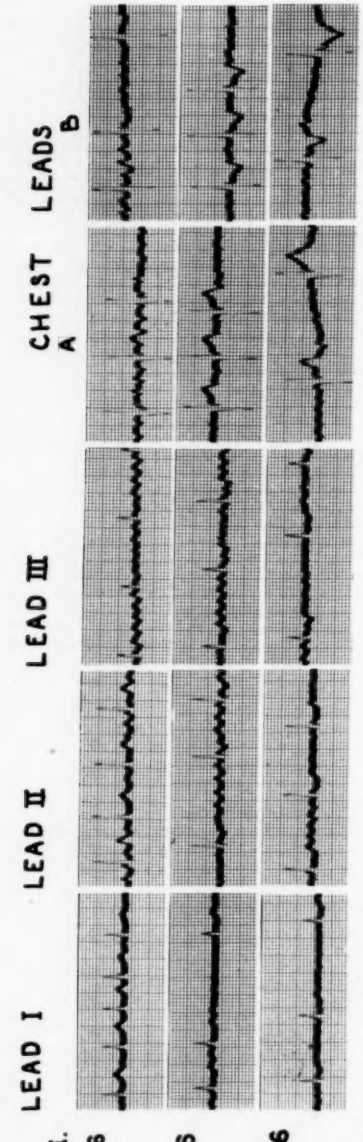

Fig. 7.—In this figure the electrocardiograms of G. MacF. (Case 18) are reproduced. The records in this case illustrate the change that occurred in one instance in which positive T-waves in the chest lead increased in amplitude after the administration of digitalis. This patient received 1.8 gm. of digitalis between 8:00 A.M. and 9:00 P.M. on Feb. 26, 1936. He was then kept on a maintenance dose of 0.2 gm. daily for the remainder of the period of study.

When maintenance amounts of digitalis were given the alterations in the form of the chest lead usually became more marked. On the other hand, the T-wave returned toward its predigitalization configuration in the five instances (Cases 4, 6, 8, 24, and 29) in which maintenance amounts of the drug were not given (Tables I and II).

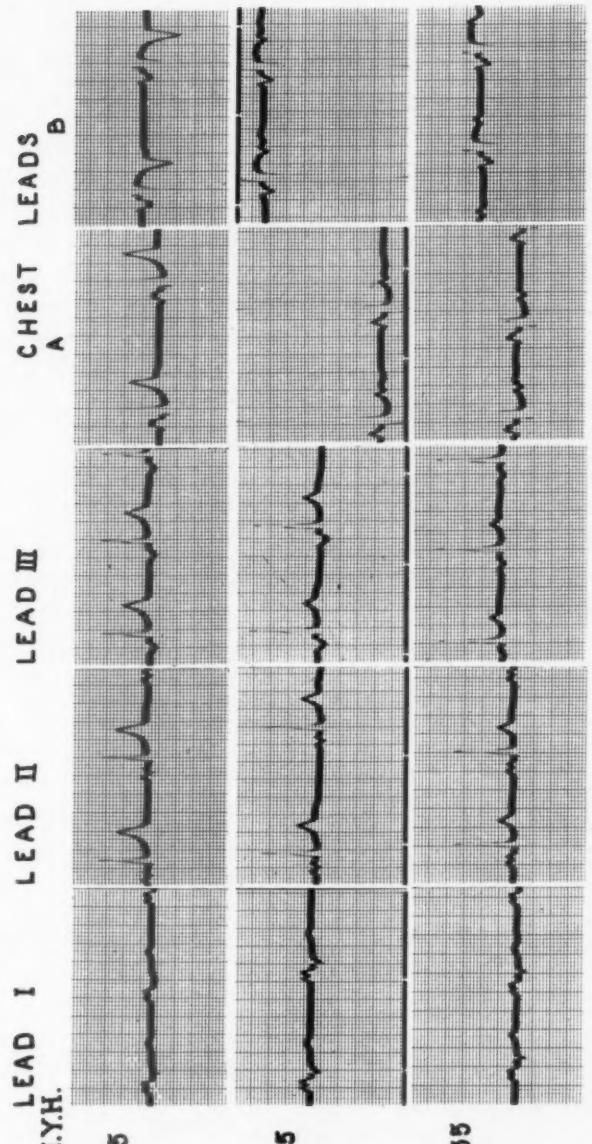

Fig. 8.—In this figure the electrocardiograms of C. W. (Case 13) are reproduced. The records in this case serve to illustrate the change that occurred in two instances. In this case positive T-waves in the chest lead became diphasic and decreased in their positive phase after the administration of digitalis. This patient received 1.8 gm. of digitalis between 8:00 A.M. and 8:00 P.M. on Dec. 20, 1935. He then received 0.2 gm. daily as a maintenance dose during the remainder of the period of study.

The changes induced by digitalis in the form of the T-waves and R-T segments in the chest lead bear close enough resemblance to those resulting from myocardial infarction and coronary artery disease to lead to confusion. In the interpretation of the chest lead effort should be made, therefore, to ascertain whether digitalis has been given.

SUMMARY

1. The administration of therapeutic amounts of digitalis induces changes in the form of the T-waves and R-T segments of the chest lead as well as the three standard leads of the human electrocardiogram.

2. In most instances after exhibition of the digitalis effect, the T-wave in the chest lead became less negative, diphasic, or positive; if already diphasic, it became less negative or increased in its positive phase or exhibited both changes; if already positive, it increased in amplitude only. The R-T segments often became less depressed, isoelectric, or elevated. However, the reverse of these changes in the T-waves and R-T segments may occur occasionally.

3. Changes in the chest lead were induced by digitalis irrespective either of the etiologic type of heart disease or of the state of cardiac compensation, a fact which has already been established for the three standard leads.[2, 4]

4. The changes induced by digitalis in the form of the T-waves and R-T segments of the chest lead may resemble those resulting from coronary artery disease or recent coronary occlusion and lead to confusion in the interpretation of the record if it is not known that the drug has been given.

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Department of Clinical Reports

AN ATTEMPT TO OBLITERATE THE PATENT DUCTUS ARTERIOSUS IN A PATIENT WITH SUBACUTE BACTERIAL ENDARTERITIS*

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OF ALL the complications of heart disease none is of more interest than *Streptococcus viridans* infection, and this equally whether one considers the nature of the invading organism, the structural changes in the heart necessary for its gaining a foothold, or the hopelessness of treatment. Although this complication is most commonly seen in relation to chronic rheumatic heart disease, its relative incidence is far greater in certain types of congenital heart disease. Thus in Abbott's series[1] of 92 cases of simple patency of the ductus arteriosus, death was caused by bacterial endarteritis or endocarditis in no less than 21. Recovery from this complication is extremely rare[2] as there is no specific medical treatment. For this reason heroic measures are often justified. The following report is an account of what we believe is the first attempt on record to obliterate the patent ductus arteriosus in a patient with *Streptococcus viridans* infection.

CASE REPORT

C. McK., a pleasant tempered young woman, twenty-two years of age, entered the Evans Memorial Hospital on Feb. 19, 1937, complaining of weakness and nausea. Although frail when a child, she had never suffered from any serious illness. At the time she began school, her parents were told by the school physician that she had a heart murmur. However, except for becoming short of breath a little more readily than her companions, she never had had symptoms related to her heart. Three months before hospital entry she began to complain of easy fatigability and malaise. Shortly thereafter she was found to have a temperature of 100° F. and was advised to go to bed. She soon developed intractable nausea and vomiting and, some time later, attacks of sharp pain in the chest which were aggravated by deep breathing and coughing. She gradually lost weight and strength and, shortly before admission, began to raise blood-streaked sputum.

Physical examination revealed a rather poorly developed, undernourished individual. The skin was pale, warm, and dry. No petechiae were found. The heart was not enlarged although the outer border of percussion dullness in the second and third left interspaces exceeded the normal. The heart rate was 104 a minute, and the rhythm was regular. In the second interspace to the left of the sternum there was heard a loud, continuous murmur with systolic accentuation. In the same area

*From the Evans Memorial and the Thoracic Surgery Service of the Massachusetts Memorial Hospitals.

there could be felt a thrill accompanying the systolic phase of the murmur. At the several valve areas no murmur was heard save the systolic phase of the continuous murmur which was widely transmitted. The pulmonary second sound was accentuated and was much louder than the aortic second sound. The blood pressure was 90 mm. Hg systolic and 60 mm. diastolic. The venous pressure was normal. The lungs were clear and resonant. The abdomen was soft. The liver and the spleen were not palpable. There was no clubbing of the fingers or the toes.

Teleroentgenograms of the chest showed several areas of soft infiltration throughout both lung fields; the heart was not enlarged, but there was moderate dilatation and increased pulsation in the region of the pulmonary artery. The electrocardiogram was normal save for slight inversion of the T-waves in Leads II and III. Blood studies revealed a slight leucocytosis and a moderate achromic anemia. Repeated blood cultures were positive for the *Streptococcus viridans*. Examination of the urine revealed a very slight trace of albumin and rare granular casts but no red blood cells.

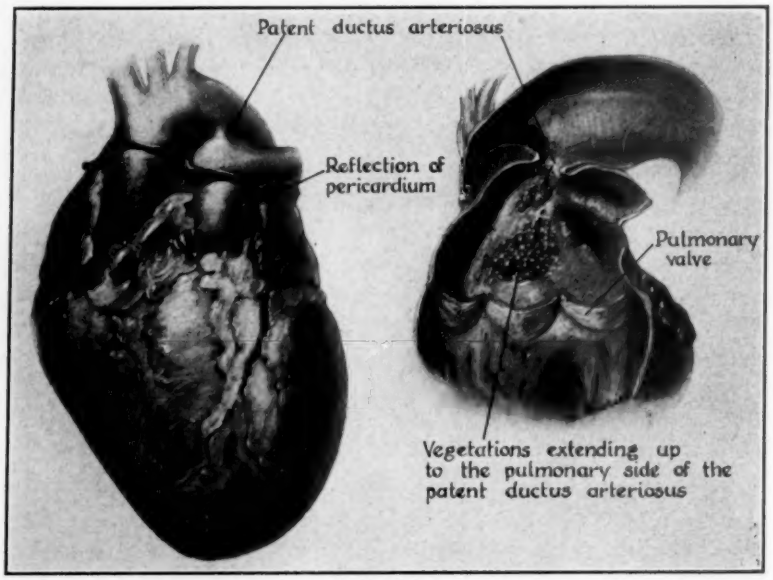

Fig. 1.

A diagnosis was made of congenital patency of the ductus arteriosus complicated with *Streptococcus viridans* infection. It was believed unlikely that there was any additional congenital or acquired heart lesion. Because there was nothing of value to offer in the way of medical treatment, the idea of attempting to obliterate the patent ductus by surgical means had some appeal. After considerable discussion the matter was broached to the patient and her parents, and the operation undertaken with their full approval.

Operation was performed March 16, 1937. After exposure of the pulmonary conus and the root of the aorta the patent ductus was readily identified. It seemed approximately 1 cm. in length and 0.5 cm. in diameter. A strong thrill was felt when a finger was placed directly on the vessel. It could be occluded easily with digital pressure, and this had neither any appreciable effect on the heart's action nor did it alter the blood pressure. The ductus was freed by blunt dissection for about three-fourths of its circumference anteriorly, laterally, and mesially. How-

ever, the right pulmonary artery was so intimately bound to it by fibrous tissue that any effort to free the posterior portion seemed extremely hazardous. Consequently an attempt was made to obliterate the ductus with a series of plicating sutures. This resulted in a considerable reduction in the lumen of the vessel but obliteration was not complete. No attempt was made to evert and suture the pulmonary artery at the pulmonary opening of the ductus. The wound was closed without drainage.

The patient's postoperative course was remarkably uneventful till within an hour of her death. She continued to feel well until the evening of the fourth day when she suddenly vomited 200 c.c. of sour-smelling yellowish fluid and quickly became cyanotic and pulseless. The blood pressure could not be obtained. Gastric lavage was without beneficial result, and despite stimulation the patient died within an hour. The immediate cause of death was acute dilatation of the stomach.

Autopsy.—The post-mortem examination was limited to the thoracic contents. The wound was uninfected and there was no evidence of hemorrhage. The pleura was intact, and there was only a little pleural transudate. The lungs showed many scattered small infarcts; in the center of a few of the larger ones there was softening and necrosis. The heart weighed 220 gm. The pericardium, myocardium, and valves were normal. One centimeter above the right anterior leaflet of the pulmonic valve, the wall of the pulmonary artery presented a friable yellowish-gray papillary vegetation measuring about one centimeter in diameter (Fig. 1). A similar vegetation, 3 mm. in diameter, was situated at the pulmonary orifice of the ductus arteriosus which was patent and had a lumen approximately 3 mm. in diameter and a length of approximately 1 mm. The length of the ductus consisted almost entirely of the thickness of the walls of the aorta and pulmonary artery, which were contiguous at this point. The stomach, as seen through an incision in the diaphragm, was acutely dilated and occupied the greater part of the abdominal cavity.

DISCUSSION

It is of most interest to consider this case in the light of those conditions which must be fulfilled before there is any hope of cure. These conditions include accuracy in diagnosis, limitation of the bacterial lesions to the ductus and the immediately adjacent portion of the pulmonary artery, the feasibility of surgical intervention,* and recovery from operation.

The diagnosis of patent ductus arteriosus, when not associated with other congenital abnormalities, should ordinarily offer little difficulty. The continuous murmur with systolic accentuation, and the thrill, such as were observed in the present case, together with the x-ray evidence of dilatation and increased pulsation in the region of the pulmonary artery, make the diagnosis. However, in those instances where additional congenital cardiac abnormalities are present, the diagnosis may present difficulties.

*On May 6, 1907, in a paper[3] before the Philadelphia Academy of Surgery, John C. Munro of Boston proposed ligation of the patent ductus arteriosus. He had made dissections on cadavers of newborn infants and proposed to split the sternum and to place a tie around the ductus or to crush it. Munro felt that the ductus was largely intrapericardial, and his operation approached it by opening the pericardium. So far as can be ascertained there is no record of his ever having attempted it on the living. He felt the operation was justifiable in cases of impending death from circulatory disturbances "with a reasonable basis for believing that the duct will be open."

If the bacterial vegetations are present in places other than in the immediate vicinity of the ductus, their removal or destruction is probably impossible. An exception to this may be the removal of vegetations from the pulmonary artery by means of a modified Trendelenburg operation. Unfortunately, a survey of the pertinent medical literature reveals only one instance[4] in which the bacterial vegetations were limited to the pulmonary orifice of the ductus and only a few instances in which the lesions were limited to the ductus and the pulmonary artery. However, it must be remembered that these data represent the findings at death, and it is surely possible that for a considerable time before death the vegetations may be confined to the neighborhood of the patent ductus. Apparently the infection nearly always begins in relation to the pulmonary orifice of the ductus, often extending to the pulmonary valves, but rarely into the aorta.[5] Hence a correct diagnosis must be made very early or there can be little hope of successful surgical intervention.

In the present case operation was not feasible because of the extensive bacterial vegetations in the pulmonary artery. The operation as performed would not even have allowed the destruction of the vegetations in the ductus itself. However, in any future attempt an effort should be made not only to obliterate the ductus itself but also the adjacent portion of the pulmonary artery. This procedure might be successful in removing all the vegetations from direct contact with the blood stream and in allowing the natural defense forces to kill the bacteria.

SUMMARY

1. Nearly one patient in four with patency of the ductus arteriosus dies because of subacute bacterial endocarditis or endarteritis.

2. In the case herein reported an attempt was made to destroy the bacterial vegetations by obliteration of the ductus.

3. The difficulties attending an operation of this nature are discussed.

4. In selected cases removal or obliteration of the patent ductus arteriosus should be attempted before the appearance of a serious degree of heart failure or subacute bacterial endocarditis or endarteritis.

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THE CLINICAL DIAGNOSIS OF TRICUSPID STENOSIS

Confirmatory Report of a Case Diagnosed Ante Mortem*

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IN A previous publication in the American Heart Journal[1] we discussed the clinical diagnosis of stenosis of the tricuspid valve, enumerating the various abnormal physiologic phenomena associated with this valvular defect, and presented a detailed report of a case in which the clinical signs of tricuspid stenosis were demonstrable. This follow-up report deals with the subsequent course of the patient's illness and the necropsy observations which substantiated the clinical diagnosis.

Clinical Course.—At the time of our previous report, the patient, a young married woman twenty-four years of age (No. U 2105), had been last seen in the Out-Patient Department May 26, 1935. At that time the clinical diagnosis was "chronic rheumatic heart disease with mitral stenosis and insufficiency; tricuspid stenosis and insufficiency; and cardiac hypertrophy and dilatation, functional Group IIb."

. Earlier electrocardiographic studies had shown various arrhythmias, including paroxysmal nodal tachycardia, nodal rhythm, nodal ectopic beats, and auriculoventricular dissociation. Large notched P-waves in Leads I and II, and right axis deviation, had been present in all tracings showing normal rhythm. Auricular and ventricular hepatic pulsations had been consistently present except with nodal rhythm, when only the systolic pulsations had been demonstrable.

The patient had always been cyanotic and subject to dyspnea, particularly during attacks of nodal tachycardia, but she had never been orthopneic or edematous. Attacks of nodal tachycardia were satisfactorily prevented or controlled by the administration of quinidine sulfate.

From June 14, 1935, to Nov. 1, 1935, her course was uneventful except for two attacks of nodal tachycardia lasting from four to six hours, both of which were terminated promptly by a few additional doses of quinidine sulfate. During this period she performed her ordinary household duties despite advice to the contrary.

On Nov. 27, 1935, she was admitted to the University of California Hospital with an acute upper respiratory infection. Dyspnea and cough were quite bothersome, and cyanosis had increased somewhat. There was a slight elevation of temperature during the afternoon for the first three days, but none thereafter. Numerous coarse râles were heard over both lungs, but these had practically disappeared at the time of her discharge from the hospital, Dec. 4, 1935. An electrocardiogram made at this time showed the presence of auriculoventricular dissociation (she had had no digitalis) and roentgenologic studies indicated that the heart had increased in size in all dimensions since the last preceding examination. There was no roentgenographic evidence of pneumonia. Except for the arrhythmia which was present during auriculoventricular dissociation, physical examination showed no changes in the heart. The systolic and diastolic murmurs over the mitral and tricuspid areas were easily distinguished. The blood pressure was 100/88. Blood

*From the Division of Medicine, University of California Medical School.
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cultures were negative. It was thought that she had had a mild attack of congestive cardiac failure which had been precipitated by the acute upper respiratory infection.

The patient was seen again in the Out-Patient Department Feb. 7, 1936, at which time she was very uncomfortable. Her pulse rate was 168 per minute, and there was no arrhythmia. An electrocardiogram revealed the presence of nodal tachycardia. The dose of quinidine sulfate was increased to 0.4 gm. two or three times a day, and she was sent home and advised to stay in bed until her cardiac rate became normal. On February 28, 1936, when she was seen next, she told a story of having had, two weeks previously, a sudden attack of severe sharp pain originating between the scapulae and radiating bilaterally and anteriorly to the sternum and down both arms. She had been taken to the emergency hospital, where a "hypodermic injection" was administered, resulting in immediate relief of this distress. No cough, tachycardia, or increased dyspnea had accompanied this attack. On examination at this time she appeared thin and pale, and complained of severe dyspnea. The lungs were normal. The cardiac findings were unchanged; the heart rate was 104 per minute. The blood pressure measured 100/70. The liver was enlarged and tender. Double pulsations were plainly palpable in the liver and visible in the superficial cervical veins.

On March 30, 1936, she entered the University of California Hospital with the history of sudden onset of paralysis of the entire right side of the body several days after her last visit to the Out-Patient Department. She had been unconscious for twenty-four hours and had experienced motor aphasia for several days thereafter. The aphasia disappeared gradually, but weakness of the right side of her body persisted. Occasionally she had had cough with small quantities of blood-stained sputum. The degree of dyspnea had remained about the same.

On examination at this time she was found to have orthopnea and marked acrocyanosis. There was a right facial nerve palsy of the supranuclear type. The lungs were normal except for a few crepitant râles at both bases. The heart was enlarged both to the right and left. The left border of dullness in the sixth intercostal space was 14 cm. from the midsternal line, and the right border in the same interspace was 4 cm. from the midsternal line. A presystolic thrill was palpable at the apex. A low-pitched presystolic murmur and a louder high-pitched systolic murmur were heard at the apex. Over the lower portion of the sternum there was a well localized, short, high-pitched diastolic murmur, and a loud systolic murmur. The pulmonic second sound was accentuated. The heart was beating regularly at a rate of 90 per minute. The blood pressure measured 94/70. The edge of the liver was palpable 4 cm. below the right costal margin, and double hepatic pulsations were plainly palpable. The left arm and leg were normal, but a 30 to 50 per cent diminution of muscular power was present on the right side. Except for loss of the abdominal reflexes on the right side, all of the reflexes were normal. Examination of the urine and blood showed nothing abnormal.

An electrocardiogram made March 30, 1936, showed pronounced right axis deviation, with high, broad P-waves in Leads II and III, notching of the P-wave in Lead I, and diphasic T-waves in Leads II and III. The mechanism was normal, and the rate was 83 a minute. Electrocardiograms made April 6 and 10, 1936, showed very little change except for slowing of the rate and the irregular appearance of premature nodal beats. Simultaneous electrocardiograms and hepatic pulse tracings which were obtained April 10, 1936 (Fig. 1), at a time when ventricular ectopic beats were numerous, showed that the latter produced no auricular wave in the hepatic pulse.

Roentgenologic studies disclosed progressive enlargement of the transverse diameter of the heart, and great enlargement of the right auricle (Fig. 2). There was considerable pulmonary congestion, but no evidence of pleural effusion.

The patient was kept in bed and treated with quinidine sulfate. She showed remarkable improvement during her stay in the hospital and was discharged April 12, 1936.

She was seen again Aug. 21, 1936. At this time she was feeling very well and had gained 10 pounds since she left the hospital. There were no significant signs

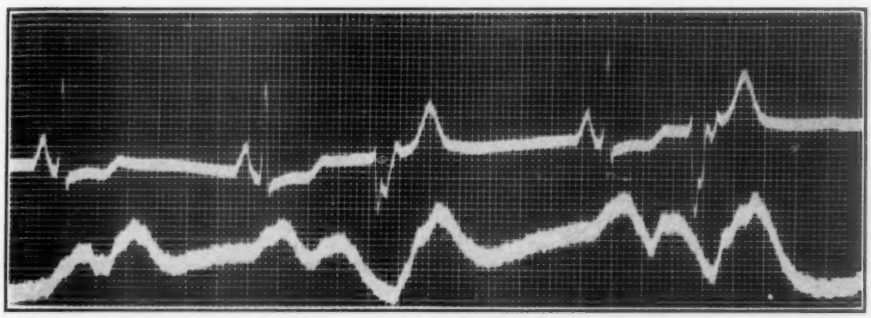

Fig. 1.—Simultaneous electrocardiogram (Lead II) and hepatogram illustrating the disappearance of the auricular wave in the hepatic pulsations during ventricular extrasystoles.

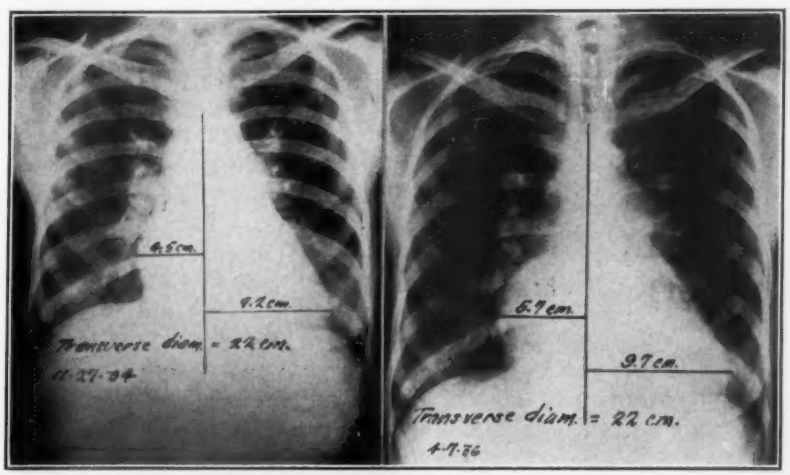

Fig. 2.—Roentgenograms illustrating the progressive increase in the transverse cardiac diameter, with marked enlargement of the right auricle.

of the previous hemiplegia, and she had experienced rapid heart action only once since her last examination. On Jan. 8, 1937, she reported again to the Out-Patient Department, stating that she had been getting along unusually well, although she had lost several pounds in weight. There were no changes in the physical findings.

On Jan. 28, 1937, the patient died at home of lobar pneumonia. Permission to make a post-mortem examination of the chest and thoracic organs was obtained.

*Necropsy Observations.**—Upon removal of the breast plate, the mediastinum was seen to be shifted slightly to the right.

*By Dr. James F. Rinehart, of the Department of Pathology, University of California Medical School.

Each pleural cavity contained approximately 200 c.c. of fluid. The lungs were crepitant except at the bases; the lower lobe of the right lung was consolidated. The lower lobe of the left lung showed very little that was abnormal. Microscopic examination of the parenchyma of the right lower lobe revealed changes typical of lobar pneumonia in the stage of red hepatization. There were no noteworthy changes in the left lung.

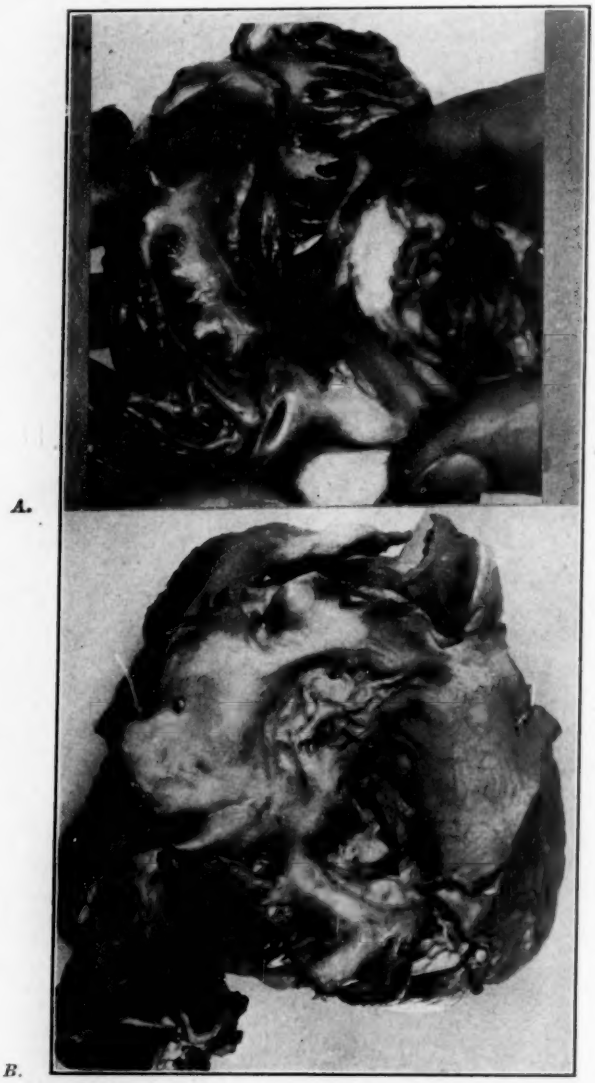

Fig. 3.—The post-mortem appearance of the tricuspid and mitral valves viewed from the right and left auricles, respectively.
A, tricuspid valve.
B, mitral valve.

The pericardium was considerably infiltrated with fat, and the cavity contained about 60 c.c. of clear yellow fluid, but there were no adhesions.

Prior to removal, the heart measured 15 cm. from its right to its left border. The left border was approximately at the left anterior axillary line, and the right

border extended about 4 cm. to the right of the midsternal line. The entire organ was dilated, but weighed, despite the obvious enlargement, only 350 gm. The auricles were twice the normal size and moderately hypertrophied. The average thickness of the auricular wall was 1 cm. The myocardium was firm, and the right ventricle was hypertrophied and dilated. The wall of the right ventricle measured 7 mm. in thickness, and that of the left, 14 mm. There was a small area of fibrosis in the apical portion of the right ventricle just beneath the epicardium. Additional areas of fibrosis were seen in the region of the auriculoventricular node immediately above the tricuspid valve and around the sinoauricular node. The leaflets of the tricuspid valve were fused and thickened, with verrucous granulations studding the line of closure. The valve was incompetent and moderately stenotic. Its circumference measured 11.5 cm. at the base and 8.2 cm. at the line of closure (Fig. 3). Thickening and fibrosis of the mitral valve had reduced its orifice to a rigid crescentic buttonhole about 1.5 cm. in diameter and 5 cm. in circumference (Fig. 3). The left ventricle was slightly dilated, and its wall was only slightly thicker than that of the right ventricle. The aortic valve measured 5 cm. in circumference and showed a very slight diffuse thickening but did not appear to be significantly affected by the rheumatic process. One of the aortic leaflets was fenestrated in its lateral margin. The pulmonary valve was not grossly abnormal; it measured 7 cm. in circumference. The chordae tendineae were thickened, partly fused, and shortened. The papillary muscles were both hypertrophied and flattened. The aorta showed scattered, slightly elevated yellowish atheromatous nodules extending from the valve to the arch. The coronary vessels were patent and elastic. There were no auricular thrombi. (This is of interest because the hemiplegia, which this patient had had several months before death, had been attributed to the loosening of a left auricular thrombus.)

Histologic examination of the myocardium showed areas of fibrosis with a few small round cells and plasma cells. The fibrosis in the right ventricle extended into the endocardium, which appeared somewhat thickened.

There was considerable edema of the tricuspid valve with much chronic inflammatory cellular infiltration at its base. In the free portion of the valve there were numerous small hemorrhages and several fairly limited areas of round cell infiltration with fibrosis and hyaline degeneration. The rheumatic process was relatively active in the tricuspid valve, as evidenced by a proliferative valvulitis and a recent hyaline verrucous lesion at the closure line. Sections of the mitral valve presented a similar appearance except that there was greater degeneration of the connective tissue with evidences of hyalinization and calcification.

Because of the various nodal arrhythmias which this patient had had, sections were taken from the region of the auriculoventricular node; they showed a mildly active rheumatic involvement of the auricular endocardium. There were a few small Aschoff bodies in the adjacent cardiac musculature.

SUMMARY

This supplementary report covers the later clinical course and autopsy findings in a case of acquired tricuspid stenosis in which the diagnosis was made ante mortem and confirmed by autopsy.

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Department of Reviews and Abstracts

Selected Abstracts

Opitz, E., and Smyth, D. H.: Blood Flow Through the Kidney During Stimulation of the Carotid Sinus. Arch. f. d. ges. Physiol. 238: 633, 1937.

As a supplement to the studies of Hartmann, Orskov, and Rein (abstract AM. HEART J., Vol. 13, p. 385, 1937) the blood flow to the kidneys was studied in dogs during stimulation of the carotid sinus nerves before and after denervation. In spite of the fall in systemic blood pressure, the flow of blood through the kidneys remained relatively constant in contradistinction to that through the fore leg, where it was increased. This was true after denervation of the kidney as well as before. An example of the automaticity of regulation of blood flow to the kidney, which is independent of its nerves, is demonstrated. Records of simultaneous curves of blood flow (Rein strohmuhr) through renal vein and brachial artery and systemic arterial pressure are reproduced.

STEELE.

Springorum, W.: Regulation of the Circulation in Skin Influenced by Local Heat. Arch. f. d. ges. Physiol. 238: 644, 1937.

Using his previously developed technique of measuring blood flow to the skin by means of a Rein strohmuhr placed upon the auricular artery of a dog, Springorum shows that vasodilatation by local heat does not alter the effectiveness of adrenalin. From this fact he concludes that an acetylcholine-like substance is not responsible for vasodilatation due to heat. The argument is reinforced by the fact that neither acetylcholine nor histamine gives rise to further increase in blood flow when the arterioles are already dilated by local heat. He concludes further that the blood flow during local heat is not governed by the rate of metabolism.

STEELE.

Bacq, Z. M.: Studies on the Physiology and Pharmacology of the Autonomic Nervous System: XXV. The Rôle of the Liver and Abdominal Viscera in the Destruction of Adrenalin. Arch. internat. de physiol. 45: 1, 1937.

The effect of injecting identical amounts of adrenalin into the crural veins of cats upon contraction of the nictitating membrane or of the virgin uterus was recorded on smoked drums before and after evisceration and before, during, and after arrest of the circulation to the viscera. The degree of contraction was either unchanged or so little increased after either procedure that the increase could be ascribed to reduction of the cellular mass through which the adrenalin was distributed. The author concludes, therefrom, confirming the work of Markowitz and Mann, that the viscera play no rôle in the destruction of adrenalin in vivo.

STEELE.

Enger, R., Gerstner, H., and Sarre, H.: Dependence of Renal Blood Flow Upon Ureteral Pressure. Zentralbl. f. inn. Med. 58: 865, 1937.

Ureteral pressure was induced in anesthetized dogs by cannulating the ureter and leading the tube therefrom into a graduated cylinder in which any desired atmospheric

pressure could be obtained. Optical records of simultaneous tracings of arterial pressure, renal blood flow (Rein strohmuhr), and ureteral pressure during the procedure were made.

Eight successful experiments were performed. Only slight, perhaps negligible, changes in renal flow occurred below 40 to 60 mm. Hg. From there on up, decrease in blood flow was rapid, falling frequently to one-third of the original value at ureteral pressures of 120 mm. Hg. Urine ceased to flow at from 40 to 70 mm. Hg. When urine secretion was allowed to take place against a manometer, without artificial increase in pressure, it was within this range of pressure (40 to 70 mm. Hg, usually about 60) that urine flow ceased. The authors note that this pressure is just at the point at which renal blood flow begins to decline and suggest that ureteral obstruction in patients may interfere with the blood flow.

It is interesting to note that in the two records produced, the arterial pressure rose slightly in one and fell abruptly in the other.

STEELE.

Menne, Frank R., Beeman, Joseph A. P., and Lobby, Daniel H.: Cholesterol-Induced Arteriosclerosis in Rabbits, With Variations Due to Altered Status of Thyroid. Arch. Path. 24: 612, 1937.

Rabbits fed pure cholesterol over a long period under different conditions, namely, (a) under normal conditions (controls), (b) following thyroidectomy and reduction in metabolism, as well as after administration of iodine to inhibit thyroid function, and (c) during administration of desiccated thyroid in such a manner as to produce intermittent periods of progression and regression in metabolism, all acquired atherosclerosis in varying degrees. In the rabbits under normal conditions, but to a greater extent in the rabbits with a depressed metabolic rate (due to removal of the thyroid or to administration of compound solution of iodine) the production of such lesions was readily accomplished. The authors conclude that the results tend to corroborate the major contention of Leary, that there are two primary conditions necessary to the development of atherosclerosis, (a) an excess of cholesterol or cholesterol esters in the blood and (b) the stress due to mechanical factors in the circulation.

MONTGOMERY.

Konschegg, T., and Monauni, J.: Quantitative Measurements of the Adrenalin Content of the Vasopressor Substance. Ztschr. f. klin. Med. 131: 99, 1936.

The authors found that adrenalin can be split off from the vasopressor substance obtained from blood and colorimetrically determined. In renal hypertension it was found that the content of adrenalin obtained in this way was markedly increased. In essential hypertension the adrenalin values were only slightly higher than in normals.

KATZ.

Petersen, H.: Rhythmic Spontaneous Contractions in Vessels. Ztschr. f. Biol. 97: 378, 1936.

The spontaneous contraction in isolated vessel strips is a reaction to stretch In an isolated artery, the sudden increase of pressure by 70 mm. Hg is followe 1.6 seconds later by a further increase in pressure which seems to be in the natur of a response to the stretch stimulus.

KATZ.

Petersen, H.: Electrical Changes Recorded From Arterial Strips of Mammal. Ztschr. f. Biol. **97**: 393, 1936.

Electrical records are obtained in such isolated arteries when they are contracting rhythmically. The electrical evidence precedes the mechanical by 8 to 10 seconds and lasts 30 seconds. They have a magnitude of 0.5 to 3 millivolts.

KATZ.

Gremels, H.: Disturbances of the Energetics of the Mammalian Heart. Arch. f. exper. Path. u. Pharmakol. **182**: 1-54, 1936.

Continuous infusion of insulin and glucose causes a massive and long lasting decrease in oxygen consumption and with it an increased efficiency of the heart. Acetylcholin also has a similar effect which is aided by the bradycardia. Adrenalin and sympatol increase work and make the heart more efficient. Small doses of adrenalin inhibit oxygen consumption.

KATZ.

Battro, A., and Lanari, A.: Injection of Acetylcholine Into the Carotid Artery of Man. Compt. rend. Soc. de biol. **125**: 541, 1937.

Acetylcholine was injected into the common carotid artery of seventeen individuals. No untoward accidents occurred. The injection was followed by a remarkable series of events: (1) immediately by hyperpnea and sometimes cough lasting one-half to one minute, (2) then by the nervous phenomena of motor agitation with occasional deviation of the eyes to the side opposite the injection, also lasting about a minute, (3) by homolateral vasodilatation of the face, neck and conjunctivae lasting from ten to fifteen minutes, (4) inconstant bradycardia and in three cases transient auricular fibrillation, neither of which occurred if atropine had been previously injected, (5) homolateral myosis, sweating, and lacrimation. He discusses briefly the site of action of the drug in eliciting the various phenomena.

STEELE.

Wezler, K., and Goyert, Kl.: A Method for Testing the Function of the Carotid Sinus Mechanism. Ztschr. f. Kreislaufforsch. **29**: 241, 1937.

A new procedure for estimating the function of the carotid sinus nerves in man is described. The measures of degree of function are obtained from simultaneous records of pulse waves from the carotid, radial, and femoral arteries and consist of the following: 1. The duration of the basic period of oscillation of the carotid artery, a function which increases with decrease in pressure within the artery, is taken as a measure of degree of stimulation of the pressor receptor nerves. 2. The ratio of the velocity of the pulse wave in the muscular arteries (for the most part brachio-radial) to the aorta is taken as a measure of the degree of contraction of the smooth muscle of the arteries. 3. The ratio of duration of systole to the interval between pulse beats is taken as an estimation of the reflex action upon the heart. For varying the degree of carotid sinus stimulation the authors vary position of the individuals studied from lying to upright. It is interesting to note that the velocity of the pulse wave in the muscular arteries as compared with that in the aorta is much greater when the individual is standing than when the individual is lying down.

In previous work Wezler has developed the thesis that contraction of the muscular coat of an artery makes the arterial wall more distensible, i.e., reduces the velocity of the pulse wave. On the basis of this theory he concludes from the present study: (1) With decrease in carotid pressure, inferred from the decreased frequency of the basic oscillation of the wall, the smooth muscle of the muscular arteries contract,

(2) and the ratio of systole to the interval of the pulse as well as the frequency of the pulse increases. From these two conclusions he draws the inference that a high degree of arterial sympathetic tone is associated or bound up with a high degree of vagal or parasympathetic tone.

STEELE.

Moon, Virgil H.: Shock, Its Mechanism and Pathology. Arch. Path. 24: 794, 1937.

Shock is a circulatory deficiency, not cardiac and not vasomotor in origin, characterized by decreased total blood volume, decreased volume flow and by hemoconcentration. An imposing array of evidence from diverse sources supports the interpretation that substances absorbed from injured tissue produce progressive circulatory deficiency by their effects on the minute vessels in systemic areas. Under the influence of these substances, and of other agents, the capillaries and venules become atonic and dilated, and their walls become abnormally permeable to the fluids of the blood. This results in stasis and leakage of fluid from the vessels. It also increases the volume capacity of the vascular system, reduces the total volume and the volume flow of the blood, increases its concentration, and produces edema. The evidence does not support the idea that local loss of blood and/or fluid at the site of injury is an adequate explanation for shock. But such a loss of fluid is a factor. It contributes to the circulatory deficiency in proportion to the volume of blood and fluid lost.

MONTGOMERY.

Hadorn, W.: Effect of Insulin and Hypoglycemia on the Heart (as Shown in Schizophrenic Patients Treated With Insulin). Ztschr. klin. Med. 130: 643, 1936.

This study is based on 43 schizophrenics without heart disease, who received large doses of insulin. During hypoglycemia, there occurred tachycardia, blood pressure rise, arrhythmias, and electrocardiographic changes. The electrocardiographic changes consisted of S-T depression, flattening or inversion of T, and prolongation of QRST and of the QRS complex. These heart changes are reversible; hence the author believes that there is no permanent heart damage from the insulin treatment.

KATZ.

Enger, R., and Arnold, H.: The 1:2-Nitrosonaphthol Reaction in Hypertensive Patients and Persons With Normal Blood Pressure: I. Blood Studies. Ztschr. f. klin. Med. 130: 725, 1936.

A negative nitrosonaphthol reaction was obtained in specially treated blood in normals, in essential hypertension, in amyloid nephrosis with marked renal insufficiency, and in acute nephritis. A positive reaction was found in chronic hypertensive nephritis and in malignant nephrosclerosis.

KATZ.

Rich, Arnold R., and Duff, G. Lyman: The Production of Hyaline Arteriolosclerosis and Arteriolonecrosis by Means of Proteolytic Enzymes. Bull. Johns Hopkins Hosp. 61: 63, 1937.

Arteriolar lesions having the characteristics of hyaline arteriolosclerosis occur at the site of injection of tryptic enzymes of animal or plant origin into the subcutaneous tissues of normal dogs. Previous medial hypertrophy or intimal proliferation is essential for the production of these changes. Whether the enzymes act directly upon the vessel wall or whether the lesion results from the action of products of protein decomposition is at present undetermined.

HINES.

Ludwig, H.: Experiments on Hydromechanics and Hemodynamics: IX. Pulse Wave Velocity in Health and Disease. Ztschr. f. d. ges. exper. Med. **99**: 352, 1936.

Because of variability in pulse wave velocity, studies must be based on a large series of observations. The author used a Müller electrical transmitting carbon capsule and determined carotid-femoral and carotid-brachial transmission times. The velocity in the arm vessels (carotid-brachial) and the aorta (carotid-femoral) increase with age. After the age of 50 years the aortic pulse wave velocity accelerates faster than that of the arm vessels. The deviations in the readings from average at any age group is as high as 50 per cent, the mean deviation being 18 per cent. On the average, pulse wave velocity tends to increase with cardiac acceleration and elevation of diastolic blood pressure. In hypertension the carotid-femoral pulse wave velocity becomes very high (maximum value 22.2 m./sec.). The acceleration is greater in essential than in renal hypertension, indicating marked alterations in the aorta in essential hypertension. In heart insufficiency the pulse velocity decreases.

KATZ.

Hecht, H., and Korth, C.: The Q-T Interval of the Electrocardiogram. Ztschr. f. Kreislaufforsch. **29**: 577, 1937.

The Q-T interval represents the duration of the excited state of the heart and is related to the duration of the heart cycle. Its duration is not always related to mechanical systole. In 24 patients with tetany and very low Ca content the duration of Q-T is lengthened. This can be reversed by calcium injections. In one case with high calcium content (ostitis fibrosa generalisata) the Q-T interval was shortened. In normal individuals Q-T is shortened by calcium injections.

KATZ.

Hollmann, W., and Hollmann, H. E.: New Electrocardiographic Methods of Investigation. Ztschr. f. Kreislaufforsch. **29**: 465, 1937.

The authors describe two methods of evaluating the variable factors that influence the electrocardiogram, viz., (1) the heart's position in the body, (2) the rotation of the electrical vector during the heart cycle, and (3) the distortion of the electrical axis by the relative muscle mass of the two ventricles. The first method consists in recording the "absolute cardiogram" which registers the changes of potential without regard to the direction of the potential. This can be done either for the frontal plane mapped by the standard three leads or for the three dimensional currents. This can be done by mathematical handling of the potentials of the several leads or by an integrating device. In this way, they have shown that the potentials registered during the heart cycle are all in one direction, the small initial and final deflection being merely the result of the direction assumed by the electrical axis when they are registered.

The second method consists in obtaining the actual record of the vector written by the resultant potential developed during the heart cycle. For this purpose a special cathode ray oscillograph was designed with six instead of four pole pieces (60° apart) to control the direction of the electron stream writing on the fluorescent screen. Each lead, I, II, and III, activates a pair of these pole pieces (180° apart). The result is a standing wave, which can be photographed and which gives the spatial value of the moving vector during the heart cycle. This they call the "triograph." By having moving instead of stationary film, a time record of the triogram is obtained from which the direction of rotation of the triogram can be determined.

KATZ.

Burkhardt, Edward A., Eggleston, Cary, and Smith, Lawrence W.: Electrocardiographic Changes and Peripheral Nerve Palsies in Toxic Diphtheria. Am. J. M. Sc. **195**: 301, 1938.

Serial electrocardiograms were made on 140 patients showing evidence of toxic diphtheria; 28 of these showed changes in the contour of the electrocardiograms.

The electrocardiographic changes were divisible into two groups comprising (a) alterations in the T-wave and (b) alterations in the conduction system.

Twenty-three patients showed the T-wave changes occurring between the fifth and thirty-ninth day of illness. A majority of the changes occurred between the eighth and fifteenth day of illness.

Seventeen patients showed conduction changes between the fifth and thirteenth day of illness; 11 of these patients developed A-V dissociation. This complication invariably proved fatal.

Fourteen patients showing electrocardiographic changes died of toxic diphtheria; seven of these received large doses of diphtheria antitoxin on or before the fourth day of illness. Early administration of antitoxin did not save this group of patients.

Peripheral nerve palsies occurred in 65 per cent of the patients presenting electrocardiographic changes. The paralysis apparently bore no causal relationship to the cardiac phenomena.

There was a rough parallelism between the conductivity as shown by the electrocardiogram and the microscopic changes in the myocardium as demonstrated in the seven cases of this series that were autopsied.

The essential histologic changes in the myocardium due to toxic diphtheria are shown to be progressively, edema, congestin, cellular infiltration, degenerative changes in the muscle fibers, and ultimate fibrosis.

These lesions found at autopsy suggest that diphtheria may be one of the causes of chronic fibrous myocarditis in patients who survive the more toxic state.

The electrocardiographic findings constitute an important guide in the treatment of diphtheria. Complete inactivity is recommended for those showing abnormal electrocardiograms until the electrocardiogram has had ample opportunity to return to normal.

AUTHOR.

Ostrowski, W., and Pines, I.: Electrocardiographic Changes in Pericardial Tamponade. Ztschr. f. d. ges. exper. Med. **101**: 465, 1937.

A parallelism between the electrocardiographic changes and the degree of pericardial effusion was found in experimental tamponade. The electrocardiographic changes are characteristic. The S-T segment is depressed and T becomes inverted. Cardiac ischemia is produced only when the effusion is rapid and large, but there always is interference with the inflow to the heart.

KATZ.

Herkel, W., and Weber, A.: Clinical and Experimental Studies of the Electrocardiogram. IX. Course of the Action Potential on Chest Wall. Ztschr. f. klin. Med. **131**: 603, 1937.

The authors found that after the Q portion of QRS the greatest negativity on the thorax anteriorly is near the middle of the base of the heart. Then it rapidly spreads toward the right base and anterior wall of the right ventricle. Invasion ends first

in the middle of the heart. It takes place then in the following order: apex, right base, and, last, middle of the base. This is based on simultaneous recording of six leads by means of amplifiers and oscillographs.

KATZ.

Hegglin, R., and Holzmann, M.: Clinical Significance of Prolonged Q-T Interval. Ztschr. f. klin. Med. **132**: 1, 1937.

Electrical systole was correlated with cycle length. In one group with prolonged Q-T, a decreased serum calcium was found, viz., tetany, spasmophilia, uremia, hepatic coma, and sprue. In this group there was a regular prolongation of Q-T when the calcium in the serum was below 9 mg. per cent, and a return to normal duration was indicated when the calcium content rose.

A second group of prolonged Q-T was found without a decreased calcium content. In this group there were (a) hypertrophied hearts on a hypertension basis and myocardial infarction, (b) diphtheria, pneumonia, and tuberculosis, and the Q-T prolongation was a sign of a serious outlook, (c) diabetic and hypoglycemic coma, (d) disturbances like myxedema, hyperadrenalemia with adrenal cortical tumors, or (e) some instances of lung emboli.

In the group with a lowered calcium content, prolongation of Q-T occurred involving chiefly the S-T interval; in the nonhypocalcemic group there was primarily a broadening of T. The latter form is the more serious, the authors believe.

KATZ.

Weber, A.: Clinical and Experimental Studies of the Electrocardiogram. X. The Meaning of the Electrocardiogram. Ztschr. f. klin. Med. **132**: 153, 1937.

The author points out that in man one really never gets a unipolar lead since the chest electrode is removed from the heart; even on the heart one gets a potential difference of two electrodes. The potential on the surface of the body is about one-sixtieth of that on the surface of the heart. The small size of the deflection on the surface of the body is not due to a drop in the potential from the center to the periphery, but is an expression of the small potential differences between various spots on the body surface. Evidence is given to show that S-T and T depression is due to damage to one ventricle.

KATZ.

Barber, Hugh: Trauma of the Heart. Brit. M. J. Feb. 26, p. 433, 1938.

The forms of heart disease which have been recorded as the result of direct violence to the chest wall or as the result of strain are discussed. The conclusion is drawn that the physical signs on examination are of little assistance in assessing the diagnosis of trauma. Reliable clinical histories, in the widest sense of those terms, must be assessed with judicious care. This includes such evidence as the patient's own doctor can supply.

The clinical diagnosis of a contusion of the heart is discussed.

It is claimed that there is clinical evidence that the normal heart may become diseased as the direct result of overstrain from effort.

With regard to these two conditions, contusion of the heart and primary cardiac overstrain, it is difficult to obtain the proof that the symptoms in question are due to a genuine heart disability, but the probabilities in some cases are sufficient to justify the diagnosis.

AUTHOR.

Bacal, H. L., and Struthers, R. R.: The Organization of a Rheumatism Service. Canad. M. A. J. 38: 227, 1938.

The organization, both medical and physical of the "rheumatism" service in the Children's Memorial Hospital, Montreal, is described. The benefit both to the staff and to the patients of continuous observations by one group interested in a study of this disease is obvious. Of these benefits, one of the most marked is the freedom from repeated respiratory tract infections enjoyed by a moderately isolated group in a humidified atmosphere.

From these observations it may be concluded that the next advance in the study of rheumatic disease in childhood must come from the study of the bacteriology of this affection.

AUTHORS.

McEwen, Currier: Cytologic Studies on Rheumatic Fever. III. A Comparison of Cells of Subcutaneous Nodules From Patients With Rheumatic Fever, Rheumatoid Arthritis and Syphilis. Arch. Path. 25: 303, 1938.

The predominant cells of syphilitic subcutaneous nodules differed strikingly from those of rheumatic and rheumatoid arthritic nodules in their reaction to supravital staining and proved to be the distinctive stimulated monocytes and clasmatocytes previously shown to be characteristic of syphilitic lesions. Thus cytologic proof is added to the evidence provided by ordinary histologic study that the clinically similar subcutaneous nodules of rheumatoid arthritis and syphilis are pathologically dissimilar; the latter are shown to be not merely nonspecific lesions but representative of syphilitic tissue reactions in general. This result gives indirect support to the belief that in rheumatic fever, too, the subcutaneous nodules are characteristic of granulomas elsewhere in the body and that conclusions drawn from a study of cells of the nodules are applicable also to those of the cardiac lesions.

In contrast to the findings in the syphilitic lesions, the cells of nodules from patients with rheumatoid arthritis were in all essential features the same as those of orthodox rheumatic nodules. Obviously, this does not prove the identity of rheumatic fever and rheumatoid arthritis, but it does add one more bit of evidence to the clinical and histologic similarities suggesting a relationship between these two diseases, and, when taken into consideration with other histologic features, it indicates that at least in the proliferative phase of the tissue reaction they are similar.

A comparative study is reported of supravitally stained preparations of subcutaneous nodules from patients with rheumatic fever, rheumatoid arthritis, and syphilis. The cells of rheumatoid arthritic nodules were found to have essentially the same characteristics as those of rheumatic fever. The cells of syphilitic nodules differed and proved to be those characteristic of syphilitic lesions in general.

AUTHOR.

Kaump, Donald H., and Dry, Thomas J.: Pulmonary Arteriolar Sclerosis. Arch. Int. Med. 61: 1, 1938.

Arteriolar sclerotic changes in the pulmonary arterial tree are more effective in producing right ventricular hypertrophy than are sclerotic changes in the larger parts of the pulmonary arterial tree. In all except three of the sixteen cases in which only the pulmonary artery and its main branches showed atherosclerotic changes, hypertrophy of the right ventricle was absent. Of thirteen cases in which there were varying degrees of diffuse pulmonary arteriolar sclerosis, hypertrophy of the right

ventricle was present in eleven. Hypertrophy of the right ventricle is, in these cases, probably an indication of elevation in blood pressure within the pulmonary artery. A close analogy exists between pulmonary arterial hypertension and peripheral arterial hypertension, in that sclerosis of the arterioles is a more common accompaniment of hypertension than sclerosis of arteries is.

MONTGOMERY.

Bonnet, B., and Bonamour, G.: Periodically Recurrent Hemorrhages of the Vitreous in Arterial Hypertension at the Time of the Menopause. J. de méd. de Lyon, No. 413: 177, 1937.

Three cases of long-standing arterial hypertension are reported with development of difficulty in vision at the onset of, and during, the menopause, due apparently to hemorrhages into the vitreous humor. Associated arterial changes were usually noted in the retina and elsewhere. The three reported cases were over fifty years of age, but the authors make the statement that this syndrome is also seen following artificial menopause at an earlier age.

STEELE.

Scheid, G., and Stern, A.: Transcerebral Iontophoresis of Bee Poison in Arterial Hypertension. Klin. Wchnschr. 33: 609, 1937.

Proceeding on the theory that narrowing of the arteries to the vasomotor centers and consequently reduction in blood flow may be the cause of hypertension the authors believe that falls in arterial pressure obtained in hypertensive patients even up to twenty-four hours after treatment were due to the dilating effect on the cerebral vessels of bee poison introduced by transcerebral iontophoresis. The current used was from 2 to 5 Ma. for fifteen minutes driven from forehead to nape of neck from lead electrodes.

STEELE.

Oppenheimer, Enid Tribe, and Prinzmetal, Myron: Rôle of the Arteries in the Peripheral Resistance of Hypertension and Related States. Arch. Int. Med. 60: 772, 1937.

A study was made of the brachial-digital pressure gradient for subjects with low, normal, and high blood pressure. Similar studies were also made for the patient with paroxysmal hypertension due to adrenal pheochromocytoma and for four patients with obstructive vascular disease. The average brachial-digital pressure gradient for patients with chronic hypertension was found to be approximately the same as for those with a normal or a low blood pressure. For three patients with very high blood pressures, there was a notable reduction in gradient. Since there is no increase in the gradient in hypertension, it is concluded that there is no increased resistance in the arteries larger than the digital arteries. For the patient with pheochromocytoma with epinephrinemia the pressure gradient was markedly increased, indicating constriction of arteries larger than the digital arteries. For four patients with obliterative vascular disease the pressure gradient was also increased, owing to obstruction in the arteries resulting from organic changes. This increase in pressure gradient, contrasted with the normal or perhaps decreased gradient of chronic hypertension, supports the view that in hypertension there is no increased resistance in the larger arteries.

MONTGOMERY.

Stalker, L. K., and Pemberton, J. deJ.: Arteriovenous Fistula: Report of a Case. Proc. Staff Meet., Mayo Clinic **12**: 557, 1937.

A case of acquired arteriovenous fistula in a boy, 15 years of age, is presented. There was marked hypertrophy of the leg on the affected side, which is unusual in arteriovenous fistula of the acquired type. There was occlusion of the femoral vein by an organized thrombus just proximal to the fistulous communication which impaired the return flow of blood and resulted in marked venous engorgement of the limb. The fistula was treated by ligation of the vessels above and below the fistulous process, and excision of the segment of artery and vein including the fistulous tract.

HINES.

Allen, E. V., and McKechnie, R. E., Effect of Intermittent Occlusion on the Circulation of the Extremities. J. Lab. & Clin. Med. **22**: 1260, 1937.

A study of the effects of intermittent venous occlusion on the skin temperatures of nineteen patients with or without occlusive arterial disease did not disclose evidence of significant or consistent vasodilatation resulting from the procedure.

AUTHOR.

Miura, O.: Concerning a Poisonous Mushroom "Clitocybe acromelalga" Ichimura and the Disease Similar to Erythromelalgia Produced by It. Tohoku J. Exper. Med. **31**: 1, 1937.

Three cases are reported in which redness, sensations of pricking, tickling, and eventually pain in the extremities followed ingestion of mushrooms *(Clitocybe acromelalga)*. Exposure to cold or heat increased the various sensations. One patient recovered in approximately ten days. The second, a sickly individual from childhood, developed edema, pustular eruptions, and ulcers of the legs, after the initial symptoms of burning and redness, and died apparently about one month after eating the mushrooms. In the third patient, too, edema and ulceration of the skin of the feet, with loss of sufficient tissue to necessitate skin grafts, followed the original redness and pain, but he eventually recovered. Histologic study of skin from this individual showed massive edema of the papillary layer and extreme widening of the papillary and subpapillary vessels, which were filled to bursting with blood. Mild thickening of the epidermis and considerable increase in pigmentation of the basal cells were also noted.

Perhaps the most interesting observation was the marked polycythemia which developed in the two cases in which counts of the red blood cells were made. One reached a level of 10.26 millions on the ninth day following the ingestion of the mushrooms and fell off by the thirteenth day to 5.56 millions. The maximum in the second case was 7.1 millions on the sixth day.

The pharmacologic action of the mushroom is then discussed, and its similarity to ergot is pointed out. The disease produced in man by its ingestion is likened to Weir Mitchell's disease (erythromelalgia), but the author makes clear that in the former the patient recovers while the latter is a chronic affliction. Because in one case local anesthetization of the nerves was followed by improvement, he believes that the disturbances of the circulation are due to the effects of the plant upon the vasomotor nerves.

STEELE.

Yater, Wallace M.: Maintenance of the Functional Integrity of Occluded Large Arteries as Demonstrated by Thorotrast Arteriography. Am. J. M. Sc. 194: 372, 1937.

Arteriography is teaching us many things about the mechanics of the circulation in vascular disease which are not demonstrable otherwise. In Case 1 we see how nature restored the function of a main artery by sidetracking the blood from above an occluded portion of the artery through a branch and bringing it back to the main trunk below. Undoubtedly other collateral arteries aided in this restoration. The history suggests embolism, but more probably sudden thrombosis occurred. The restorative alterations were made within a month of the time of occlusion.

Case 2 is quite different from Case 1. Here the occlusive process apparently developed very slowly, being due to gradual diminution of the lumen by atherosclerosis. But again we see the same detour of the blood through smaller arteries back to the main artery. Case 3 was similar to Case 2 in that the occlusive process was undoubtedly a very slow one due to atherosclerosis.

Readjustment of the circulation of the lower extremity by direct anastomosis allows one to make a better prognosis than in cases in which the main arteries are completely obliterated and in which the circulation is entirely dependent upon smaller vessels. In Cases 1 and 3 there was no gangrenous process, and in Case 2 trophic changes were minor and healed readily.

In cases of embolism in which recovery ensues, it may be that the circulation in an extremity is reestablished in the manner described, at least at times. Arteriectomy as advocated by Leriche may be efficacious in that such a procedure conceivably may stimulate the development of direct anastomoses as well as the collateral circulation in general.

Only one illustration of a case similar to these could be found in the literature. This was Case 20 (p. 377) of Demel, Sgalitzer and Kollert. It is probable, however, that such cases have been observed in large clinics where arteriography is frequently employed.

It is believed that most collateral vessels are merely enlarged and elongated branches that existed prior to the onset of vascular disease. Such cases as those described indicate that at times new anastomoses may develop, however, since it is quite improbable that a branch of an artery normally empties into the same artery a short distance below its origin.

AUTHOR.

Cust, Norman: Symmetrical Peripheral Gangrene Following Scarlet Fever. M. J. Australia 2: 880, 1937.

A single case is presented. A two-year-old boy developed gangrene of both feet seventeen days after the onset of a scarlet fever rash. Tight swelling of the feet and lower legs immediately preceded the gangrene and was believed to have caused the gangrene by pressure. Both feet were icy cold. A large bruise on the left thigh, a bleeding time of seven minutes, and a platelet count of 36,000 was taken as evidence that purpura may have been the cause of the swellings. Both limbs were amputated just below the knees nearly three weeks after the onset of gangrene, with no trial of incision for relief of pressure. Reexamined a year after his illness he was well and free from further purpura.

MONTGOMERY.

Lambie, G. G., and Morson, S. M.: Acrocyanosis. M. J. Australia 2: 1070, 1937.

A single case of acrocyanosis is presented in detail. Arms, legs, and cheeks were especially involved. This case is unusual in that it is of a young woman with

disturbances of bodily growth, metabolism, and mental development. Also, seven close relations had chilblains of the extremities. The patient's symptoms were coldness and blueness of the extremities, aggravated by cold weather, chilblains of the fingers which had ulcerated, and of the toes which had not. Considerable relief was obtained by proper protection from cold.

X-ray revealed no evidence of calcification of arteries. Heating the patient produced a skin temperature rise to the level found in normal people so treated. When blood flow through a limb was interrupted by means of a blood pressure cuff, and the part warmed, and pressure released (reactive hyperemia, Pickering test), the resultant flush occurred nearly as fast as it does in a normal person. Nerve block (ulnar) abolished the abnormal vessel reactions, over the area of nerve distribution.

The differentiation of acrocyanosis from Raynaud's phenomena was made by the following findings: the abnormality was constant (nonparoxysmal), there was no blanching or pain, and all evidence pointed to the fact that only the most distal vessels (arterioles) were affected.

MONTGOMERY.

Neurath, O.: The Determination of Circulation Time With Magnesium Sulfate. Ztschr. f. Klin. Med. **132**: 134, 1937.

The author uses 5 c.c. of 10 per cent solution of magnesium sulfate, which leads to a sudden sensation of warmth in the head. No side reactions were noted. The method of determining circulation time is the standard one. He found circulation times of 11 to 17 seconds in normal persons, 12 to 26 seconds in persons with hypertension without heart failure, and 13 to 58 seconds in persons with hypertension with heart failure. In thyroid disease the circulation time is accelerated. This is also true in paroxysmal tachycardia, except when the heart rate is above the critical value when the circulation time is prolonged. No difference was found between "right and left heart failure."

KATZ.

Heckmann, K.: The Changes in the Heart's Position During Its Pulsation and Its Appearance in the Roentgenkymogram. Fortschr. a. d. Geb. d. Röntgenstrahlen **55**: 319, 1937.

Many of the waves in the roentgenkymogram are due to position changes in the heart. This study is based on a comparison of types of curves obtained in man with those in model experiments; and also on observations of movements of a case with pericarditis calculosa. Double waves are to be explained as due to a combination of actual pulsations and changes in the heart's position.

KATZ.

Heckmann, K.: Pulsations in the Pulmonary Vessels and Their Manifestations in the Kymogram. Klin. Wchnschr. **16**: 733, 1937.

Pulsations in the region of the pulmonary artery are caused not only by this vessel, but also by the aorta. In congestion of the lesser circuit, the author finds the trapeze form in the roentgenkymogram, indicating an increased resistance to flow peripherally from the pulmonary artery; hence the decrease in the pulse occurs later in diastole. Double waves are due to interference between pulmonary and aortic pulsations when the two pulses are noticeably asynchronous. The splintering of the pulmonary wave occurs also in open ductus Botalli. This last is attributed to asynchrony of the pulses transmitted from the right ventricle and through the ductus.

KATZ.

Book Review

ARTERIOVENOUS ANEURYSM. Abnormal Communications Between the Arterial and Venous Circulations. By Emile Holman, A.B., B.A. Oxon., M.D. Professor of Surgery, Stanford University Medical School; Surgeon-in-Chief, Lane and Stanford University Hospitals. New York, 1937, The Macmillan Company, Price $5.00.

The experimental arteriovenous fistula as produced by the author is described, and this is followed by a careful study of the local manifestations as well as the effects produced upon the remainder of the circulatory system. The physiologic effects upon the circulation following the establishment of a fistula that are considered include: Fall in the blood pressure, increased cardiac contraction, increased total blood volume, and increased cardiac output. The reversal of the condition, viz., closure of the fistula, causes the blood pressure to rise again and decreases the cardiac contraction, the total blood volume, and the cardiac output. The experimental data are compared with the clinical observations. In his discussion the author has properly pointed out the effect of the fistula upon the heart, the increased surface temperature beyond the fistula, and the increase in the size of the extremity in the presence of a fistula.

Efficiently presented are the clinical examples of arteriovenous fistula, including the acquired intracranial arteriovenous aneurysms, intrathoracic arteriovenous communications, mycotic arteriovenous aneurysms, and the congenital arteriovenous communications of the peripheral vessels. The physiologic changes due to open ductus arteriosus have been elaborated upon following the experimental production of interventricular septum defects.

The physiologic problems are of fundamental importance and may be far-reaching Study of these fundamental principles may bring forth an explanation of the development of cardiovascular disease and hypertension. Although arteriovenous communications may be rare, as has been pointed out by the author, they afford an excellent opportunity for increasing our knowledge of the physiology of the mechanisms that control the circulation.